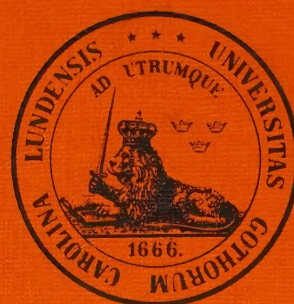


SELENOLOTHIOPHENES AND -SELENOPHENES

SYNTHESES, REACTIONS AND SPECTROSCOPIC PROPERTIES.

Andreas Konar



Lund 1980

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SYNTHESES, REACTIONS AND SPECTROSCOPIC PROPERTIES

Andreas Konar

Division of Organic Chemistry 1
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University of Lund

Lund 1980

There's this desert prison . . . with an old prisoner, resigned to his life, and a young one just arrived. The young one talks constantly of escape, and, after a few months, he makes a break. He's gone a week and then he's brought back by the guards. He's half dead, crazy with hunger and thirst. He describes how awful it was to the old prisoner. The endless stretches of sand, no oasis, no life anywhere. The old prisoner listens, then says, "Yep. I know. I tried to escape twenty years ago." The young prisoner says, "You did? Why didn't you tell me, all these months I was planning my escape? Why didn't you let me know it was impossible?" And the old prisoner shrugs, and says, "So who publishes negative results?"

Jeffrey Hudson in
"Scientist as Subject:
The Psychological Imperative."
Quoted in *Chemistry*, September 1977

to my wife

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Title and subtitle SELENOLOTHIOPHENES AND -SELENOPHENES SYNTHESSES, REACTIONS AND SPECTROSCOPIC PROPERTIES		
Abstract The preparation of the four, differently fused selenolo-selenophenes starting from selenophenes was investigated. Treatment of 2-(3-selenienyl)-1,3-dioxolane with, by turn, n-butyl-lithium, red selenium, methyl chloroacetate, sodium ethoxide and copper in quinoline, afforded <u>selenolo[2,3-b]selenophene (I)</u> in 28 % over-all yield. A similar reaction sequence starting from 2-(3-bromo-2-selenienyl)-1,3-dioxolane gave <u>selenolo[3,2-b]-selenophene (II)</u>, identical with that obtained in the reaction between acetylene and selenium. In addition, about 30 other compounds were identified among the products of this reaction, for example alkylselenophenes, alkylselenoselenophenes, biselenienyls, benzo[b]selenophene and tricyclic-fused systems. No other selenoloselenophene than II was detected. A similar approach to the third selenophene, <u>selenolo[3,4-b]selenophene (III)</u>, as to I and II, failed. III was instead synthesized in 44 % yield from 4-methylseleno-3-selenophene aldehyde by quaternizing its methylseleno group with methyl bromoacetate, cyclization to 2-carbomethoxyselenolo[3,4-b]selenophene (IV) hydrolysis and decarboxylation. IV could also be prepared by dehydration of the corresponding dihydroselenoloselenophene oxide in very low over-all yield due to the difficulties encountered in the NaHSe-cyclization of 2,3-bischloromethyl-5-carbomethoxyselenophene. 2-Carbomethoxyselenolo[3,4-b]thiophene (V), a derivative of the last, hitherto unknown "classical" selenolothiophene, was also synthesized in a similar manner. Although hydrolysis and decarboxylation of IV gave the selenophene III, only dimeric and oligomeric acids were obtained on hydrolysis of V.		
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Konar

Date August 6, 1980

Photoelectron spectra of I and II, and ^1H , ^{13}C and ^{77}Se NMR spectra of I, II and III, as well as of their selenolothiophene analogues were investigated. In the case of II, a series of 2-substituted compounds containing both strongly electron-attracting and electron-donating substituents, as well as substituents of intermediate character, was synthesized. Substituent effects in this series were investigated by ^1H , ^{13}C and ^{77}Se NMR spectroscopy. A brief survey of existing data on ^{77}Se NMR of organoselenium compounds is also given.

The reactivity of II and selenolo[3,2-b]thiophene (VI), relative to thieno[3,2-b]thiophene (VII), towards electrophilic reagents, was studied by means of competitive experiments. The reactions studied were acetylation, formylation and chlorination, and the over-all reactivity order was found to be: II > VI > VII. The reactivity ratios relative to selenophene and thiophene were also determined. The formylation and metalation of selenolo[2,3-c]thiophene (VIII) were investigated. Vilsmeier formylation of VIII gave a mixture of 4- and 6-substituted aldehydes in a ratio of 3:2. Metalation followed by formylation changed this ratio to 1:4. In addition, a product of a ring-opening reaction of a substitutional RO-II type was obtained.

The different synthetic approaches to the [3,4-c]-annealed "nonclassical" selenoloselenophenes and selenolothiophenes were described. A brief survey of existing methods for the preparation of other "nonclassical" heterocyclic systems containing a fused thiophene or selenophene ring was also given. Evidence for the existence of 1,3-dimethyl, 1,3-dicarbethoxy and 1,3-diphenyl derivatives of the selenolo-[3,4-c]selenophene system (IX), was given. The best synthetic routes to these derivatives were the acid-catalyzed dehydration of the corresponding selenoxides and the base-catalyzed reductive debromination of the selenium dibromides. Attempts to prepare the tetraphenyl derivative of IX by treatment of tetrabenzoyl ethane with P_2Se_5 in pyridine failed. However, a modified procedure for P_2Se_5 preparation, rendered the compound sufficiently reactive to effect the ring-closure of several 1,4-diketones to substituted selenophenes.

This review summarizes results from the following papers, which will be referred to in the text as A-K.

- A S. Gronowitz, A. Konar and A.-B. Hörnfeldt
On the Reaction between Acetylene and Selenium.
Chemica Scripta 10, 159 (1976).
- B S. Gronowitz, A. Konar and V.P. Litvinov
Electrophilic Substitution in Selenolo[3,2-b]selenophene
and Selenolo[3,2-b]thiophene - A Quantitative Study.
Chemica Scripta, in press.
- C S. Gronowitz, A. Konar and A.-B. Hörnfeldt
⁷⁷Se NMR Studies of Organoselenium Compounds.
V. Substituent Effects in 2-Substituted Selenolo[3,2-b]-
selenophenes Studied by ¹H, ¹³C and ⁷⁷Se NMR Spectroscopy.
Manuscript.
- D R. Gleiter, M. Kobayashi, J. Spanget-Larsen, S. Gronowitz,
A. Konar and M. Farnier
On the Electronic Effects of the Heteroatom in Five-Membered
Heterocycles. Photoelectron Spectra of Selenolo and Pyrrolo
Analogues of Thieno[2,3-b]thiophene and Thieno[3,2-b]-
thiophene.
J. Org. Chem. 42, 2230 (1977).
- E A. Konar and S. Gronowitz
Selenolo[3,4-b]thiophene - An Attempted Synthesis of the
Fourth "Classical" Selenolothiophene.
Manuscript.
- F A. Konar and S. Gronowitz
Selenolo[3,4-b]selenophene - the Third "Classical"
Selenophene.
Tetrahedron, in press.

- G S. Gronowitz, A. Konar and V.P. Litvinov
On the Vilsmeier Formylation and Metalation of
Selenolo[2,3-c]thiophene.
Izvest. Akad. Nauk SSSR, Ser. Khim., in press.
- H S. Gronowitz and A. Konar
Nonclassical Selenoloselenophenes.
J. Chem. Soc., Chem. Commun. 1977, 163.
- J A. Konar and S. Gronowitz
Nonclassical Selenoloselenophenes and Selenolothiophenes.
Manuscript.
- K S. Gronowitz and A. Konar
On the Reaction of 1,4-Diketones with Phosphorus
Pentaselenide.
Chemica Scripta 12, 11 (1977).

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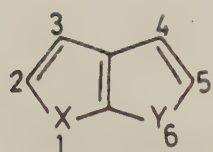
1. INTRODUCTION

Heteroaromatic systems have always intrigued organic chemists. This is partly due to a basic interest in comparing the chemical and physical properties of heteroaromatic compounds with those of the classical carbocyclic aromatics. Interest in heteroaromatic chemistry is also due to the widespread occurrence of heterocyclic compounds in nature. The main reason for the specific chemical behaviour of monocyclic heteroaromatic compounds is the presence of the heteroatom in the molecule. The heteroatom is not only an electron donor in the formation of an aromatic π -electron system but is also responsible for the direction of electrophilic and nucleophilic attacks, and the course of other chemical reactions on the heteroaromatic molecule. The situation is even more complex with the condensed systems since in this case the physical properties and reactivity of the compounds are strongly affected by both the nature of the condensed rings and the type of condensation.

The main research interest in these laboratories has for many years been focused on the chemistry of thiophene and its derivatives. Recently, the chemistry of fused thiophenes and other five-membered heterocyclic rings, such as furan and selenophene, has also been investigated.

In continuation of this research on chemistry of a variety of fused heterocyclic systems carried out at this department, the subject of this thesis is the synthesis, the chemical properties and the spectroscopic investigations of the selenium analogues of thienothiophenes, namely selenolothiophenes and selenoloselenophenes.

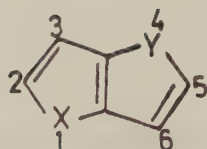
By the annelation of two five-membered heterocyclic rings with one heteroatom, four isomeric fused heterocycles may be formed if the heteroatom is the same in both rings, or five, if the heteroatoms are different. The latter, because of the unsymmetrical nature of the [3,4-b]- and [2,3-c]-annelated systems, where structures having the arrangement of the heteroatoms in both rings reversed are not identical (cf. compounds VII and VIII in Scheme I). Thus, four isomeric thienothiophenes



I X=S, Y=S

V X=S, Y=Se

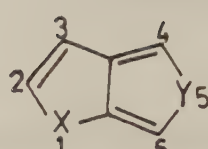
X X=Se, Y=Se



II X=S, Y=S

VI X=S, Y=Se

XI X=Se, Y=Se

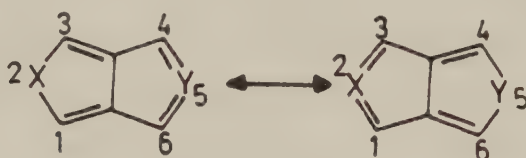


III X=S, Y=S

VII X=Se, Y=S

VIII X=S, Y=Se

XII X=Se, Y=Se



IV X=S, Y=S

IX X=S, Y=Se

XIII X=Se, Y=Se

Scheme I

I-IV or selenoloselenophenes X-XIII, but five selenolothio-
phenes V-IX, may be formed. Compounds I-IV, where X = Y = S,
are often called thiophtenes and, analogously, compounds X-XIII
with X = Y = Se - selenophtenes. The earliest reported thio-
phtene was thieno[2,3-b]thiophene (I), described by Biedermann
and Jacobson¹ in 1886. Thieno[3,2-b]thiophene (II) was first
reported by Challenger and Harrison² in 1935, and the unstable
thieno[3,4-b]thiophene (III) by Wynberg and Zwanenburg³ in
1967. The fourth, "non-classical" isomer, thieno[3,4-c]thiophene
(IV), for which the only uncharged resonance contributors are
structures containing tetravalent sulfur, is not yet known in
its unsubstituted form, but some of its derivatives have been
reported by Cava et al. (For a review, see Ref. 4 and references
therein.) A review concerning the chemistry of the isomeric
thiophtenes and related systems appeared in 1976⁵ and covers
the literature until the first half of 1974. Selenolothio-
phenes were also discussed briefly. Selenolo[2,3-b]thiophene (V)
was first reported in 1969 by Bugge,⁶ and selenolo[3,2-b]thiophene
(VI) in 1968 by Goldfarb et al.⁷ The synthesis of selenolo-
[2,3-c]thiophene (VII) was described in 1971 by Goldfarb et al.,⁸

but no report on the fourth "classical" selenolothiophene, selenolo[3,4-b]thiophene (VIII), has appeared to date. Some unstable derivatives of the "nonclassical" selenolo[3,4-c]-thiophene (IX) were, however, reported by Saris and Cava.⁹ A review concerning the synthesis and physical properties of the three selenolothiophenes V-VII was published in 1973 by Goldfarb et al.,¹⁰ concentrating upon the Russian contributions in this area. Selenoloselenophene system was first mentioned by Briscoe et al.¹¹ in 1928, but Umezawa,¹² in 1939, was first to recognize the possible existence of the three isomers X-XII and, in fact, claimed the isolation of all three as by-products in the preparation of selenophene from acetylene and selenium. Neither the fourth, "nonclassical" selenolo[3,4-c]selenophene (XIII) nor its derivatives had been reported elsewhere.

Based on the inherent differences of the above systems, the following summary is subdivided according to the type of annelation. Thus, Part 2 of this thesis is mainly concerned with the synthesis, reactivity and some spectroscopic properties of the [2,3-b]- and [3,2-b]-annelated compounds. In this part also, a detailed study of the product distribution of the reaction between acetylene and selenium is presented. In Part 3 the synthesis, reactivity and NMR spectra of the [3,4-b]- and [2,3-c]-fused systems are discussed.

The different synthetic approaches to the "nonclassical" [3,4-c]-annelated compounds are the subject of Part 4, where a brief survey of existing methods for the preparation of other "nonclassical" heterocyclic systems with a fused thiophene or selenophene ring is also given.

Throughout the summary, Roman numerals refer to compounds found in the schemes included in the text, and combinations of letters and numerals indicate in which paper a particular compound was reported. The original numbers of compounds are used throughout and copies of the Papers A-K are included after this summary.

2. THE [2,3-b] - AND [3,2-b] -ANNELATED SYSTEMS

2.1. Synthesis

Different routes leading to [2,3-b] - and [3,2-b] -fused thieno- and selenolothiophenes I, II, V and VI were reviewed by Litvinov and Goldfarb.⁵ At present, probably the most convenient and universal way to these systems is the Dieckmann cyclization of suitable ortho-bifunctional thiophene derivatives. This method has been used by Gronowitz et al.¹³ and, independently, by Goldfarb et al.¹⁴ in their preparation of thieno[2,3-b] - thiophene (I), and by Goldfarb et al.¹⁵ in the synthesis of thieno[3,2-b] thiophene (II). Selenolothiophenes have also been prepared by this procedure; selenolo[2,3-b] thiophene (V) by Bugge⁶ and selenolo[3,2-b] thiophene (VI) by Goldfarb et al.⁷

The selenoloselenophene system was first mentioned, in 1928, by Briscoe et al.¹¹ in their search of an improved synthesis of selenophene from acetylene and selenium. They isolated "a sky-blue liquid, b.p. about 240-250°, containing about 20 % of selenium, which was probably an impure specimen of selenophene, the analogue of thiophene". Umezawa,¹² in 1939, analyzed the high-boiling residue formed in this reaction and claimed isolation of the three isomeric selenophenes X, XI and XII. The structure determination was mainly based on dipole moment measurements,¹⁶ that were later shown by Gronowitz et al.¹⁷ to be erroneous. Apart from the above work, and a study of magnetic susceptibility of X and XI carried out by Japanese workers in 1943,¹⁸ there are few reports concerning selenophenes X and XI or their derivatives. Thirty years after the work of Umezawa,¹² Italian workers¹⁹ published an X-ray analysis of selenolo[3,2-b]selenophene (XI). Unfortunately, neither melting point nor the method of preparation was given and the incorrectness of Umezawa's assignments was not recognized. Thus, until the work of Gronowitz et al.¹⁷ in 1974, these assignments were generally accepted, being both cited in recent review articles on selenophene chemistry^{20,21} and the latest review on thienothiophenes and related systems, published in 1976.⁵

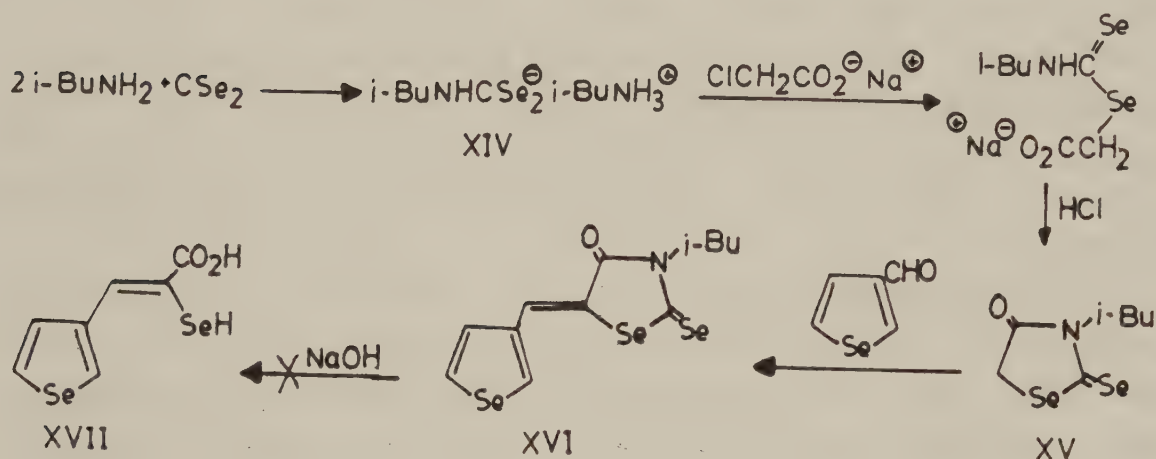
In 1974, tetrachloro derivatives of X and XI as well as of selenolothiophenes V and VI, were reported.²² Dechlorination of the last two gave the unsubstituted V and VI but, curiously, no attempts were made to obtain the parent selenophthenes X and XI in a similar way. In 1979, Goldfarb et al.²³ described the synthesis of 3-bromoselenolo[2,3-b]selenophene and, apart from the work which is the subject of this thesis, there have been no other reports on the selenophthenes or their derivatives.

Therefore, in order to obtain unambiguous evidence for their structures, the synthesis of selenophthenes X and XI, and later also of XII, was undertaken. Considering the usefulness of the Dieckmann cyclization route in preparing [2,3-b]- and [3,2-b]-fused thienothiophenes¹³⁻¹⁵ and selenolothiophenes,^{6,7} a similar approach to selenoloselenophenes X and XI was adopted in Paper A.

As starting materials, ethylene acetals of 3-selenophene aldehyde (A V) and of 3-bromo-2-selenophene aldehyde (A VIII) were used. These were reacted with n-butyllithium followed by red, amorphous selenium and methyl chloroacetate, then hydrolyzed to the intermediate formyl selenienylselenoacetates. Subsequent cyclization was achieved, without isolation, with ethanolic sodium ethoxide solution and, after hydrolysis, the acids (A VII) or (A IX) were obtained. Decarboxylation with copper in quinoline gave the parent selenophthenes X and XI in about 25 % yield, based on the starting acetals. The yields of the one-pot reactions to the acids were 45 % and 36 %, respectively.

In the search for a possible improvement of the selenophthene synthesis, an attempt was made to prepare X in a manner analogous to the synthesis of thieno[2,3-b]thiophene (I), recently reported by Schneller and Petru.²⁴ They prepared 2-carboxythieno[2,3-b]thiophene in 70 % yield, by the iodine-promoted cyclization of β -(3-thienyl)- α -mercaptoacrylic acid, which was readily available from the 3-thiophene aldehyde - rhodanine adduct. For preparation of selenolo[2,3-b]selenophene (X), a selenium analogue of rhodanine was thus required. Rhodanine is best prepared from ammonium dithiocarbamate and sodium chloroacetate, the former being obtained from the

reaction of ammonia with carbon disulfide.²⁵ As the reaction of carbon diselenide with ammonia does not lead to the corresponding ammonium diselenocarbamate, but results in polymerization,²⁶ the N-isobutyl-substituted selenium analogue of rhodanine XV was prepared from the previously described,²⁷ quite stable isobutylammonium N-isobutyldiselenocarbamate (XIV) and sodium chloroacetate, as outlined in Scheme II.

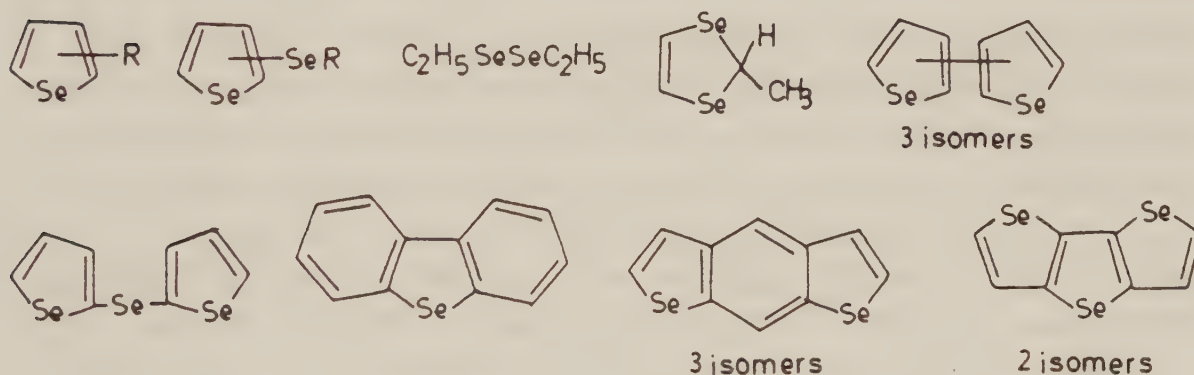


Scheme II

XV is a very unpleasant smelling, quite unstable compound but can be stored in ether solution for months without decomposition. It can also be reacted with 3-selenophene aldehyde to give the unstable adduct XVI, which unfortunately decomposes very rapidly on treatment with base. The desired acrylic acid XVII, the cyclization of which was expected to give 2-carboxy-selenolo[2,3-b]selenophene, could thus not be obtained by the route of Scheme II, which was therefore abandoned. Hence, the Dieckmann cyclization path to selenophthenes X and XI, as described in Paper A, may at present be considered as the most convenient and reliable route to these two fused heterocyclic systems.

As mentioned above, the reaction between acetylene and selenium was also reported to give rise to selenophthenes. In fact, Umezawa¹² claimed isolation of all three selenophthenes X-XII from the residue, after removal of selenophene, and the presence of selenolo[3,2-b]selenophene (XI) was also confirmed by Gronowitz et al.¹⁷

In connection with this department's work in the selenophene field, the reaction between acetylene and selenium has been carried out on a relatively large scale.²⁸ Since this reaction was reported¹² to be an alternative source of selenophthenes, a detailed study of the product distribution was undertaken, and is presented in Paper A. In addition to selenophene and the previously reported benzo[b]selenophene, more than 30 other compounds were identified, and some of them also isolated. However, in contrast to Umezawa's results, no selenophthene other than selenolo[3,2-b]selenophene (XI) could be detected among the products of the reaction. The product distribution was studied at two temperatures and is described in detail in Table I of Paper A. The classes of compounds formed are summarized in Scheme III, excluding non-selenium compounds and the above-mentioned benzo[b]selenophene and selenophthene XI.



Scheme III

2- and 3-substituted alkylselenophenes and alkylseleno-selenophenes constituted the greatest part of the low molecular weight compounds formed, 2-n-butylselenophene being the highest alkylselenophene found. The 2-substituted alkyl- and alkyl-

selenoselenophenes predominated over the 3-substituted ones. The only acyclic product detected was diethyl diselenide, and the only cyclic, but non-aromatic compound, was 2-methyl-1,3-diselenocyclopentene-4. In the higher-boiling part of the residue, benzo[b]selenophene, all three biselenienyls, some phenyl and selenienyl selenides, dibenzoselenophene and other tricyclic-fused compounds were found. Some of them were isolated by means of preparative gas chromatography and, in some cases authentic samples were prepared allowing comparison of retention times and mass spectra. Other methods of characterization were comparison of the mass spectra with published data and analysis of the fragmentation pattern of the mass spectra obtained from GC/MS. In most cases at least two different methods were employed. The complexity of the reaction between acetylene and selenium was stressed, as well as its preparative importance in preparation of selenophene and, under optimal conditions, selenolo[3,2-b]selenophene (XI).

2.2. Electrophilic substitution reactions

Electrophilic attack on thienothiophenes I and II results in 2-substituted compounds, the second electrophile attacking the other free α -position. A considerable amount of information on electrophilic substitution reactions of I and II, such as acetylation, formylation, halogenation and nitration, is now available. These reactions, as well as the isotope exchange of deuteriated thiophenes, were recently reviewed in Ref. 5.

There are, however, relatively few reports on electrophilic substitution reactions of the selenium analogues of thienothiophenes. Umezawa¹² obtained tetrabromo derivatives of selenophthenes X and XI and a 2-nitro derivative of XI, and Goldfarb et al.²⁹ studied the bromination and formylation of selenolothiophenes V and VI. Vilsmeier formylation of both V and VI gave mixtures of 2- and 5-formyl derivatives, the substitution taking place predominantly in the selenophene moiety. NBS-bromination of V gave a similar mixture of 2- and 5-bromo derivatives, but only 5-bromoselenolo[3,2-b]thiophene was

formed in the bromination of VI. Its preferential formation was assumed to be due to the primary attack of the bromine on the selenium ring atom. A similar result was also obtained in the NCS-chlorination of VI, which gave exclusively 5-chloroselenolo-[3,2-b]thiophene. This reaction is described in Paper B, which was aimed at a quantitative study of the electrophilic substitution of selenolo [3,2-b] thiophene (VI) and selenolo[3,2-b] -selenophene (XI).

Many quantitative studies on electrophilic substitution of five-membered heterocycles have been carried out and the results were reviewed in 1971 by Marino.³⁰ However, comparatively few quantitative data exist on the electrophilic substitution of compounds formed by fusion of two five-membered rings. A quantitative study of thieno[3,2-b]thiophene (II) by Bugge³¹ prompted the investigation of its selenium analogues VI and XI in Paper B. The reactions studied by Bugge³¹ were acetylation, formylation and chlorination. Choosing the same three reactions and maintaining the same experimental conditions would make a quantitative evaluation of the reactivities towards electrophilic substitution in the series XI-VI-II-selenophene-thiophene possible. Attempts to carry out deuterium exchange experiments on VI and XI failed, owing to the lability of both systems under the reaction conditions. In all three electrophilic reactions studied, the overall order of reactivity was found to be: XI>VI>II, which indicates that the known experimental data, showing a higher rate of electrophilic substitution of selenophene than of thiophene,³⁰ can also be extrapolated to include fused systems II, VI and XI. The overall reactivities of VI and XI, relative to II, varied with the nature of the electrophile in the same way as the reactivities of I and II, relative to thiophene,³¹ (in all cases the reactivity ratios increased in the order acetylation<chlorination<formylation). The three reactions gave rise to only α -substituted derivatives and thus no partial relative reactivities of β -positions could be calculated. Only the partial reactivities of the two positions of the unsymmetrical selenolo [3,2-b] thiophene (VI) were determined (except for NCS-chlorination where exclusively the 5-chloro derivative was formed). An attempt to rationalize the

results on the basis of existing quantum chemical calculations failed, since the latter gave an incorrect picture of the systems' mutual reactivities, as well as of the reactivity ratio for positions 2 and 5 in selenolo[3,2-b]thiophene (VI).

The only electrophilic substitution reaction of XI which gave rise to detectable amounts of a 3-substituted derivative was nitration, described in Paper C. This paper is concerned with NMR studies of a series of 2-substituted selenolo[3,2-b]-selenophenes, which will be the subject of the next chapter.

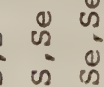
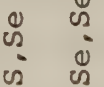
2.3. ^1H and ^{13}C NMR spectra

^1H NMR spectroscopy has found wide application in studies of unsubstituted thieno- and selenolothiophenes as well as their derivatives and the results have been reviewed by Litvinov and Goldfarb.⁵ The ^1H NMR spectra of the symmetrical thiophenes I and II and selenophenes X and XI (cf. Paper A) are of the AA'BB' type, while the spectra of the unsymmetrical selenolothiophenes V and VI are of the ABCD type. As in thiophene and selenophene, the resonances of α -protons occur at lower field than those of β -protons, with the difference increasing in the series I<V<X and II<VI<XI. The signals of both α - and β -protons are found at lower field in selenophenes than in thiophenes regardless of the type of annelation. The chemical shifts and vicinal couplings in the thiophene part of selenolothiophenes V and VI resemble those of the corresponding thiophenes, while the parameters of the selenophene part of the molecules are reminiscent of selenophenes. Long-range spin-spin interactions between protons separated by 5 or 6 bonds are observed only when the transmission takes place along a regular zig-zag path. Selenolothiophenes and -selenophenes are also characterized by spin-spin interactions between the ^{77}Se isotope of spin 1/2 and the ring protons. The coupling constants can in some cases be obtained from the ^{77}Se satellites in the ^1H NMR spectra or, alternatively from the undecoupled ^{77}Se NMR spectra and will be discussed in Chapter 2.4. All the above ^1H NMR parameters of thiophenes I-III and selenolothiophenes

V-VII have been tabulated in Ref. 5 and can now be complemented with the data for the selenophthenes X, XI and XII from Paper A, Ref. 17 and Paper F, respectively.

On the other hand, despite the huge mass of information on ^{13}C NMR spectroscopy of aromatic and heteroaromatic compounds accumulated during this decade, only ^{13}C spectra of thiophenes I and II³² and selenophthene XI¹⁷ have been reported. In Paper A, the ^{13}C NMR spectrum of selenolo[2,3-b]selenophene (X) and, in Paper F, the ^{13}C spectrum of the third selenophthene, selenolo[3,4-b]selenophene (XII), were described. The ^{13}C data of selenolo[2,3-c]thiophene (VII) is given in Paper G, but no other ^{13}C measurements of selenolothiophenes have been published. It was felt, therefore, that a tabulation of ^{13}C chemical shifts of the above systems could be of value and in order to make it complete the ^{13}C NMR spectra of the selenolothiophenes V and VI were also recorded. Their chemical shifts are included in the Table on page 18 where, for the sake of perspicuity, the ^{77}Se NMR parameters of the selenium-containing systems are also collated. These will be discussed in Chapter 2.4. A brief inspection of the ^{13}C shifts collected in the Table reveals that, in all [2,3-b]- and [3,2-b]-annelated systems, absorption of β -carbons occurs at a higher field than that of α -carbons, which was also the case for α - and β -protons. This relative order of the carbon chemical shifts is the same as of the α - and β -carbons in selenophene but opposite to that in thiophene, where the α -carbons absorb at higher field than the β -carbons (a difference of 1.7 ppm). This effect is not only retained but even more pronounced, when one regards the bridged carbons in [2,3-b]-fused systems, where C-7, situated α in both rings, absorbs 10.3 ppm, 13.5 ppm and 14.2 ppm upfield of the C-8 resonance in I, V and X, respectively. The direct coupling constants between ring carbons and their hydrogens, $^1J_{\text{C-H}}$ which are not given in the Table are, as in both thiophenes and selenophenes, greater for α - than for β -carbon atoms.

Table. ^{13}C NMR chemical shifts (ppm)^a of thiophenes I and II, selenolothiophenes V-VII and selenophthenes X-XII, and the ^{77}Se NMR chemical shifts (ppm)^b and coupling constants (Hz)^c of selenolothiophenes V-VII and selenophthenes X-XII.

X, Y	Compd. No.	C ₂	C ₃	C ₄	C ₅	C ₆	C ₇	C ₈	Se	$^2J_{\text{Se-H}}$	$^3J_{\text{Se-H}}$
	I	129.1	120.4	120.4	129.1		137.6	147.9			
	V	130.0	122.0	123.3	132.6		136.4	149.9	- 60.0	49.1	9.2
	X	133.8	124.2	124.2	133.8		136.1	150.3	- 26.1	48.8	9.6
	II	127.9	119.9		127.9	119.9	139.9	139.9			
	VI	127.7	122.6		131.7	123.4	139.5	141.6	- 84.8	47.6	7.8
	XI	131.6	125.3		131.6	125.3	140.3	140.3	- 56.0	47.0	7.2
	VII	133.0	120.8	114.9		115.2	136.4	150.7	-173.8	46.8	8.0
	XII	131.4	120.7	119.8		117.9	136.9	152.2	-176.4 (Se-1) +126.4 (Se-5)	47.1 48.1	7.0 -

^a In deuterioacetone solution at 15.04 MHz relative to TMS as an internal standard.

^b In deuterioacetone solution at 19.135 MHz relative to selenophene as an external standard.

^c Determined from the uncoupled ^{77}Se NMR spectra and/or from the ^{77}Se satellites in the ^1H NMR spectra.

The proton chemical shifts of a series of 2-substituted thiophenes I and II have been determined by Bugge,³³ who found good correlations with the corresponding shifts in thiophenes and with the reactivity constants $\mathcal{F}$ and $\mathcal{R}$ of Swain and Lupton.³⁴ This approach was also used in the ^{13}C NMR studies of a similar series of 2-substituted I and II.³²

The two-parameter equation $\delta = i + f\mathcal{F} + r\mathcal{R}$ of Swain and Lupton³⁴ divides the electronic effect of a substituent into resonance and non-resonance components. This equation has been criticized by Katritzky et al.,³⁵ who questioned the validity of the assumption on which the $\mathcal{R}$ values were calculated (zero resonance potential of trimethylammonium ion group). With this criticism in mind, the $\mathcal{F}$ and $\mathcal{R}$ values were used in Paper C, since it was believed that they can still give a qualitative indication of the relative contributions of the inductive and mesomeric effects to the substituent-caused shifts, as expressed by the coefficients f and r .

In Paper C, ^1H , ^{13}C and ^{77}Se NMR parameters for a series of 2-substituted selenolo[3,2-b]selenophenes have been determined and the substituent-caused chemical shifts compared to the analogous shifts of the corresponding thieno[3,2-b]thiophenes and -selenophenes. Great similarities were observed between the 2-substituted selenophthenes XI and thiophthenes II and good linear correlations for both ^1H and ^{13}C chemical shifts were obtained (cf. Table V in Paper C). This was perhaps not unexpected in view of the results of Paper D, where replacement of sulfur by selenium in this kind of heterocyclic system was shown to result in only slight perturbation (see Chapter 2.5.). Good correlations were also obtained for ^1H , ^{13}C and ^{77}Se chemical shifts of 2-substituted XI with the corresponding shifts in selenophenes. The slopes of the equations in Table VI in Paper C reveal that the sensitivity to substituent effects of the proton and carbon atoms in the substituent-bearing ring is of the same order of magnitude in the fused as in the monocyclic system, while in the neighbouring ring the sensitivity of both ring protons and carbon atoms is nearly halved. The chemical shifts of all ring hydrogens, and some of the carbons, could also be correlated with different types of reactivity parameters and the results are presented in Tables VII and VIII in Paper C.

2.4. ^{77}Se NMR spectra

Improvements in NMR technique in the last decade, particularly due to the advent of Fourier transform operation, have led to a great increase in NMR measurements of nuclei other than hydrogen. This is particularly true for the ^{13}C nucleus, which now rivals the proton as the most important NMR isotope. However, nearly all elements have at least one potentially valuable isotope for NMR and, indeed, most of them have now been studied.³⁶ Selenium exists as several naturally occurring isotopes, one of which, ^{77}Se , possesses a nuclear spin of $\frac{1}{2}$. The low natural abundance (7.58 %) and relative NMR sensitivity ($6.93 \cdot 10^{-3}$ that of the proton) of the ^{77}Se isotope causes the receptivity of this nucleus to be $5.26 \cdot 10^{-4}$ relative to that of the proton (but still 2.98 relative to ^{13}C). This low receptivity implied a necessity for the use of neat liquid samples in the earlier continuous wave (CW) work on direct selenium NMR, but indirect double resonance (INDOR) experiments subsequently permitted the examination of more dilute solutions.³⁷ Although this technique can only be used when protons are coupled to ^{77}Se , it has to date enabled data to be acquired for the widest range of compounds. However, for many species having complex proton spectra (e.g. aromatic compounds) the Fourier transform approach is clearly superior. The use of Fourier transform ^{77}Se NMR was, in fact, first reported by Gronowitz et al.³⁸ in 1973 and since then the ^{77}Se spectra of a variety of organoselenium compounds have been investigated in these laboratories (cf. Paper C and references therein). Attractive features of ^{77}Se NMR spectroscopy are the pronounced sensitivity of the nuclear shielding to the chemical environment (the established shift range is over 2200 ppm)³⁶ and the stereospecificity of the coupling constants.^{37,39} Two earlier reviews concerning selenium NMR have appeared, one dealing with ^{77}Se shift measurements,⁴⁰ and the other with ^{77}Se - ^1H coupling constants and proton chemical shifts in organoselenium compounds.⁴¹ The most recent and comprehensive review is that given in Chapter 12.C. of Ref. 36. Since then only a few reports on ^{77}Se NMR have appeared.

Odom et al.^{42,43} determined spin-lattice relaxation times for several classes of selenium compounds and similar studies have also been carried out by Pan and Fackler,⁴⁴ Gansow et al.⁴⁵ and Koch et al.⁴⁶ A study of the pH dependence of the chemical shift of ^{77}Se in aqueous H_2SeO_3 has been reported⁴⁷ and an investigation of the ^{77}Se NMR spectra of a series of [2,3-b]- and [3,2-b]-fused benzoselenolothiophenes and -selenophenes will appear shortly.⁴⁸ All the above studies were performed using the Fourier transform technique, while the INDOR technique was used in a recently published⁴⁹ investigation of ^{77}Se spectra of substituted selenoanisoles. There are some differences of opinion as to the most suitable reference material for ^{77}Se chemical shift determination; H_2SeO_3 , SeOCl_2 , selenophene and dimethyl selenide all having been used. While selenophene, used as an external standard in all ^{77}Se NMR work carried out in these laboratories, appears to be a suitable reference for heteroaromatic selenium compounds, dimethyl selenide has the advantage of being less toxic and more easily accessible. It is also suitable for both direct and indirect methods of detection and its chemical shift lies upfield of most classes of organic and inorganic selenium compounds. Thus, expressing ^{77}Se chemical shifts relative to dimethyl selenide and employing the usual convention of ascribing downfield shifts a positive sign would have the additional advantage of giving positive values to most of the observed ^{77}Se shifts. Consequently, this convention was adopted in Figure 1, where a comprehensive chart of ^{77}Se chemical shifts in organic and inorganic compounds is given and in Figure 2, in which the ^{77}Se shift region of heteroaromatic selenium compounds is expanded, making possible a more specific visualization of ^{77}Se shifts of the compounds that are the subject of this thesis. The shifts given in Figure 1 are taken mostly from Ref. 36, complemented with recent data from Refs. 42-49 and Papers A, C, F and G. The ^{77}Se shifts of heteroaromatics shown in Figure 2 were mainly determined in these laboratories^{17,38,50,51} and by a research group at the University of Liège.^{48,52} In Figure 2, the shifts of the unsubstituted heterocycles are indicated by an X. The shifts and ^{77}Se - ^1H coupling constants of selenolothiophenes V,⁵²

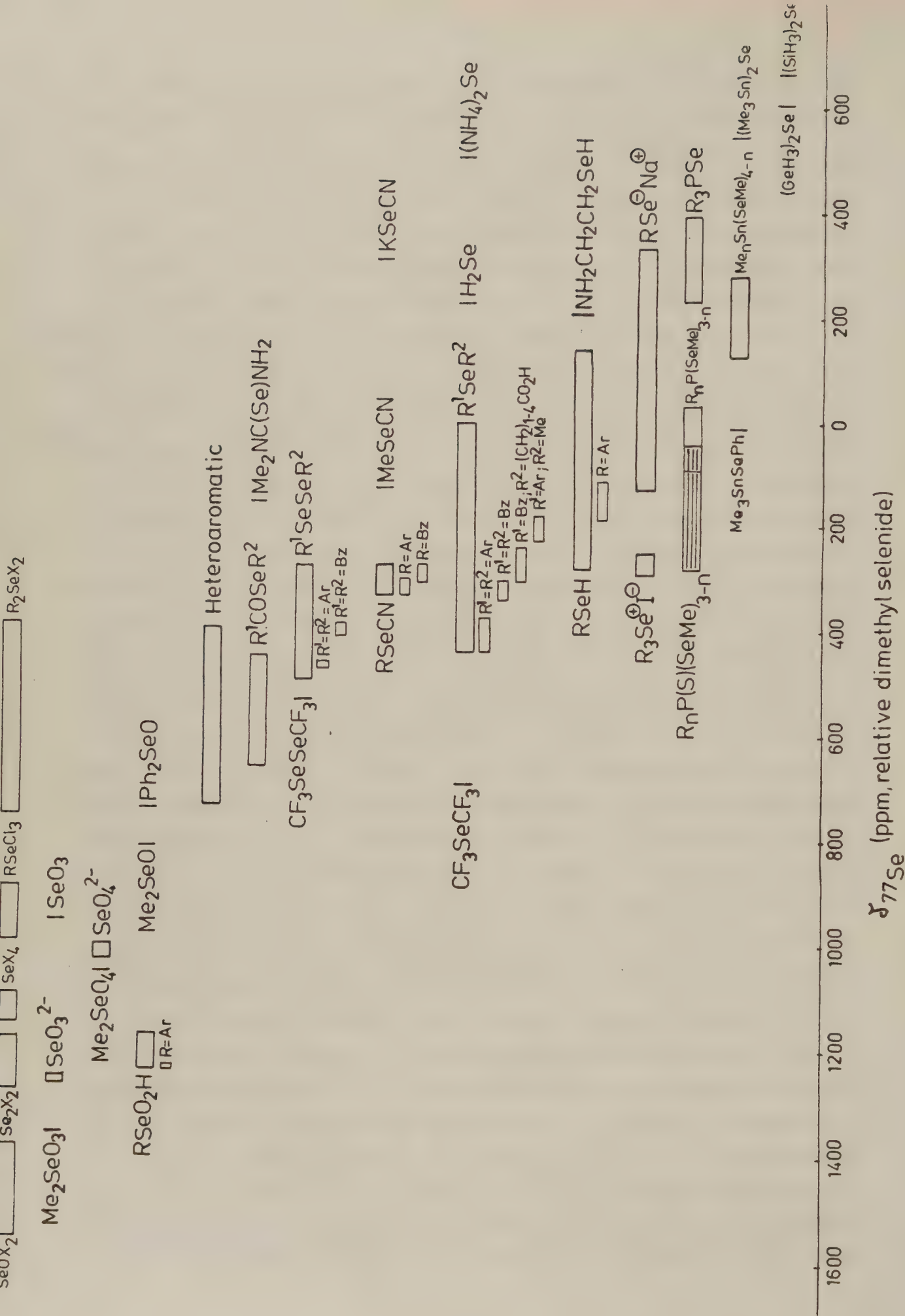
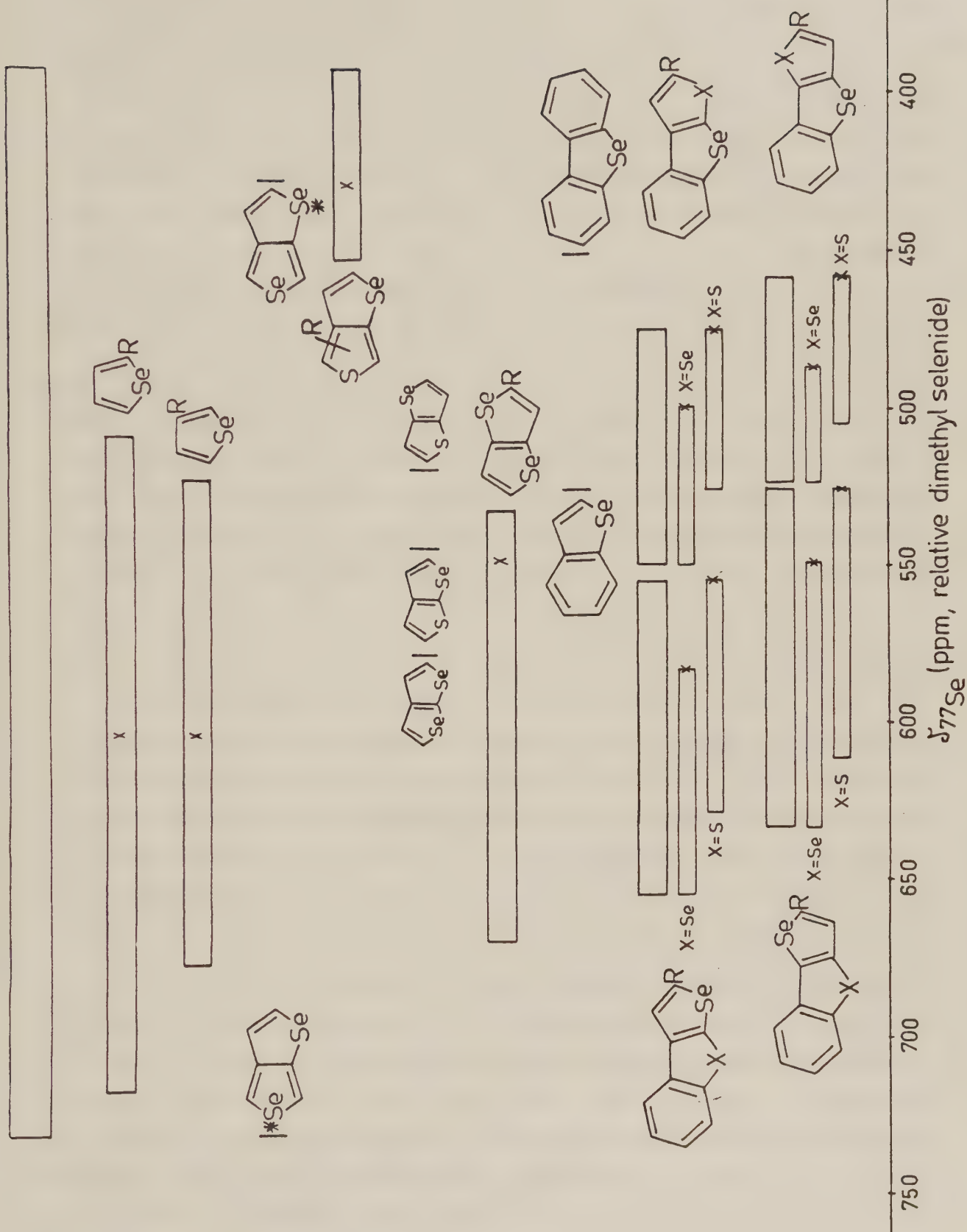


Figure 1. General ^{77}Se chemical shift chart

HETEROAROMATIC SELENIUM COMPOUNDS



⁷⁷Se chemical shifts of heteroaromatic selenium compounds

VI⁵¹ and VII (Paper G) and selenoloselenophenes X (Paper A), XI¹⁷ and XII (Paper F) are also given in the Table on page 18. A brief inspection of the effect of ring fusion on selenophenes and benzo[b]selenophenes, as presented in the Table and Figure 2, reveals that ring fusion has a shielding effect on the Se nucleus. The only exception is Se-5 in XII, which absorbs 126 ppm downfield of selenophene and, in fact, is the most deshielded selenium atom in any heteroaromatic found to date. The ⁷⁷Se NMR spectrum of XII will be discussed in Chapter 3.3.

The shielding effect of ring fusion in selenophene also appears to be dependent on the type of annelation and decreases in the series: [3,4-b] >> [3,2-b] > [2,3-b]. Moreover, the fusion of a thiophene ring has a stronger shielding effect than that of selenophene, whereas, in the tricyclic compounds, the fusion of a benzene ring appears to have a slight deshielding effect on the selenium nucleus in the lateral position.⁴⁸ However, in compounds VII and XII, fusion of a thiophene or selenophene ring has a comparable effect on the Se-1 absorption. The coupling constants between the ⁷⁷Se nucleus and the ring protons separated by two or three bonds are of the same magnitude as in simple selenophenes.⁵⁰

The effect of substituents on the ⁷⁷Se chemical shifts in different classes of organic selenium compounds has been studied^{36-38,40,48-50} and in many cases good correlations with substituent parameters have been observed. All studies confirmed the great sensitivity of ⁷⁷Se shifts to changes in the chemical environment. ⁷⁷Se NMR spectra of 2- and 3-substituted selenophenes have been investigated by Gronowitz et al.⁵⁰ and, in Paper C, a similar study of a series of 2-substituted selenolo[3,2-b]selenophenes (XI) was reported. This enabled the use of ⁷⁷Se chemical shifts as a probe for the interaction between substituents and the selenium atom not only in the substituent-bearing ring, but also in the neighbouring ring. Good correlation between the Se-1 chemical shift in 2-substituted XI and the corresponding selenophenes⁵⁰ has been obtained. As with 2-substituted selenophenes,⁵⁰ the anomalously small down-field shifts of Se-1 in the carbonyl- and nitro- 2-substi-

tuted XI were observed. If this effect, as suggested by Gronowitz et al.,⁵⁰ is indeed caused by the binding interaction between the carbonyl oxygen lone-pair and the selenium d-orbitals, it should not influence the chemical shift of Se-4 and no longer outweigh the -M effect of the carbonyl and nitro substituents. In Paper C, it was indeed shown to be the case, which indirectly corroborates the suggestion of Gronowitz et al.⁵⁰

Summarizing, it can be said that the most general trends emerging from the data presented in Figure 1 and from the interpretation of published results are the large chemical shift range of ^{77}Se (over 2200 ppm), making it a valuable analytical tool, and a substantial decrease in shielding of the selenium produced by an increase in the effective electronegativity of the substituents. It has generally been assumed that the paramagnetic term makes the dominant contribution to the ^{77}Se shielding and that $\delta^{77}\text{Se}$ correlates inversely with the calculated electron density on selenium. However, it appears that, when the atoms directly attached to selenium are charged, other factors may supervene.

2.5. Photoelectron spectra

The last decade has seen the applications of photoelectron spectroscopy (PE) to a large number of organic compounds. Numerous reviews have appeared, describing the technique and the different approaches to interpretation of the spectra. A recent review by Gleiter et al.⁵³ covers some aspects of photoelectron spectroscopy of organic sulfur compounds. Although this review is essentially confined to sulfides, thiocarbonyls and some polyvalent sulfur compounds, photoelectron data for more than a hundred sulfur compounds, many of which belonging to other classes, are collected in tabular form.

Practically all theoretical predictions of molecular PE spectra are based on canonical molecular orbital (MO) theory. The close relation between ionization energies and MO energies is largely responsible for the popularity of PE spectroscopy.

An approximation which allows PE spectroscopic data to correlate with MO energies derived for the ground state is Koopmans' theorem.⁵⁴ This large simplification involves setting the negative value of the orbital energy, ϵ_j , equal to the vertical ionization potential, $I_{V,j}$: $-\epsilon = I_{V,j}$. Koopmans' theorem is used quite often to interpret PE spectra, even though it neglects electron correlation and reorganization effects. Fortunately, the energy terms for both effects seem to cancel each other out in the case of most medium sized and large organic molecules, for which reason the theorem is a fairly good approximation for these molecules. Its validity was also assumed in Paper D for the interpretation of photoelectron spectra of selenolothiophenes V and VI and selenophthenes X and XI. Analysis of the PE spectra of these compounds was of particular interest since, together with the earlier recorded PE spectra of thiophthenes I and II,⁵⁵ it could enable a better understanding of the influence of the heteroatom in these fused systems. Thus, a qualitative description of the electronic effects operating in the series of [2,3-b]-annelated (I - V - X) and [3,2-b]-annelated systems (II - VI - XI) was made possible. The PE spectra of both series all looked very similar, which was not surprising in view of the similar electronegativities of sulfur and selenium. Replacement of sulfur by selenium can thus be considered a minor perturbation of the valence electronic system, i.e. simple perturbation theory is valid. From the above mentioned similarity of the PE spectra, the correlation diagram of the first four observed ionization potentials could be drawn (cf. Figure 3, Paper D). To check this diagram, a number of semiempirical calculations were carried out using the parametrized Hückel (HMO) procedure, the EWMO, CNDO/2 and MINDO/3 methods. Based on the HMO results, the correlation diagram of the calculated energies of the four highest occupied levels was then drawn and the shape of the most important orbitals indicated (Figure 4, Paper D). Comparison of these two correlation diagrams shows that the HMO calculations not only reproduce the significant trends in the PE spectra for these series of compounds but are also in satisfactory numerical agreement with the experimental energies. Thus, most of the observed shifts of the bands

can be understood in terms of simple first order perturbation theory applied to the HOMO's of I and II.

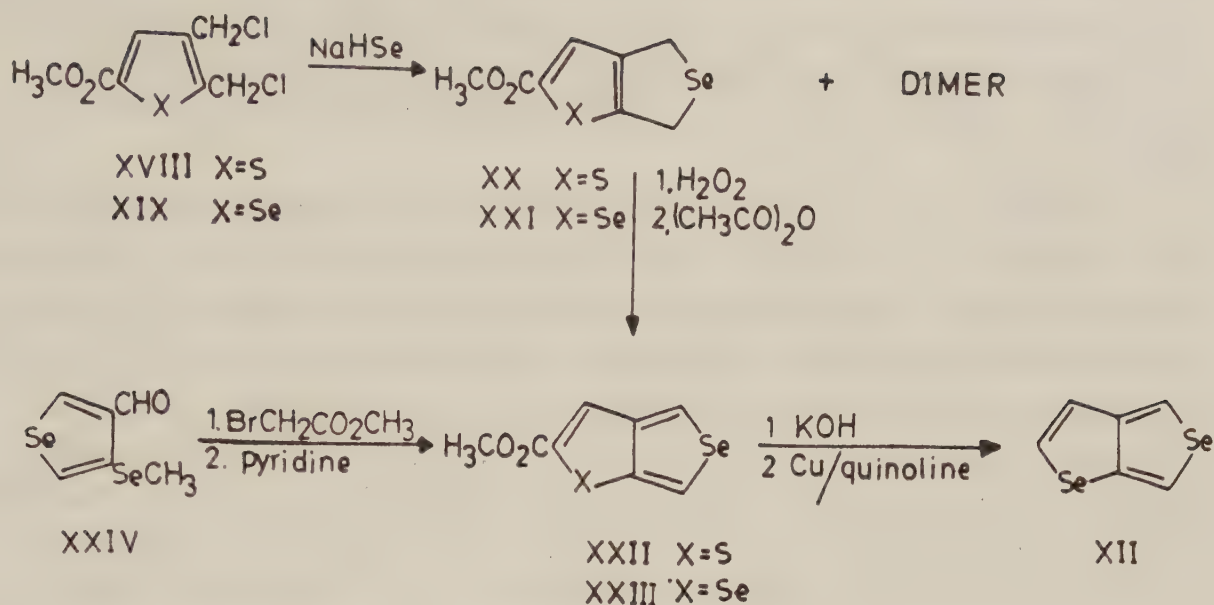
This is, however, not the case when sulfur or selenium is replaced by an NH-group, i.e. in the case of the isomeric [2,3-b]- and [3,2-b]-annelated thieno- and selenolopyrroles. The PE spectra of these systems were also studied in Paper D and it was found that the effect of such replacement on the π -electronic system is governed by a balance between the influence of the increase of the resonance integral for the bonds to the heteroatom and a strongly destabilizing inductive effect due to the polarity of the N-H bond.

3. THE [3,4-b]- AND [2,3-c]-ANNELATED SYSTEMS

3.1. Synthesis

There are few reported synthetic routes leading to thieno-[3,4-b]thiophene (III) or its selenium analogues. All of them begin with a suitable derivative of thiophene or selenophene and can, in principle, be classified according to the method of building the second heterocyclic ring onto that of the starting material. The first group comprises methods with a ring-closure step leading directly to a derivative of an aromatic, fused system. In the approaches of the other group, an initially formed, saturated ring is converted to a thiophene or selenophene by dehydration of a sulfoxide or selenoxide, or by dehydrobromination of a selenium dibromide. From the four possible systems with this type of annelation (III, VII, VIII and XII), only two have been reported, namely thieno[3,4-b]-thiophene (III)³ and selenolo[2,3-c]thiophene (VII).⁸ The presence of XII among by-products of the reaction between acetylene and selenium was claimed by Umezawa¹² but the results given in Papers A and F contradict this statement.

As mentioned in Chapter 2.1., the Dieckmann cyclization of suitably substituted thiophene or selenophene aldehydes is, at present, probably the most convenient route to thiophenes I and II, selenolothiophenes V and VI and selenophenes X and XI. This route, which is an example of the first group of synthetic approaches to III and its selenium analogues (cf. above), was also successful for the preparation of 2-carboxy-thieno[3,4-b]thiophene by Litvinov and Fraenkel,⁵⁶ who however did not attempt decarboxylation to the parent thiophene III. This was instead performed by Wynberg and Zwanenburg,³ who obtained III as an unstable, colourless oil, turning yellow rapidly on standing in air. The acid, however, was prepared by a different route, analogous to that outlined in Scheme IV and belonging to the second group of synthetic methods leading to III and its selenium analogues.



Scheme IV

Synthetic approaches along this path were also applied in Papers E and F, aiming at the preparation of selenolo[3,4-b]-thiophene (VIII) and selenolo[3,4-b]selenophene (XII), respectively. In both papers the cyclization of 2,3-bis(chloromethyl)-5-carbomethoxythiophene (XVIII) or -selenophene (XIX) turned out to be the critical step in the reaction sequence outlined. Despite numerous trials to optimize reaction conditions, the cyclizations resulted predominantly in dimers, trimers and even higher oligomers. Nevertheless, the monomeric XX and XXI could be separated from the reaction mixtures and their subsequent oxidation with hydrogen peroxide gave the selenoxides (E VIII) and (F 7). Dehydration with acetic anhydride afforded the esters XXII and XXIII of the desired aromatic systems VIII, and XII, respectively. XXII could also be obtained by dehydrobromination of the selenium dibromide of XX. An attempt to hydrolyze the ester function of XXII to the corresponding acid (E XII) resulted in destruction of the selenophene ring, the dimeric acid becoming instead a main product. If the hydrolysis was attempted at an earlier stage,

i.e. on the dihydroselenolothiophene XX, the same dimeric acid was formed along with higher oligomeric and polymeric products. Thus, the approach to the parent compound VIII along the route of Scheme IV failed, although 2-carbomethoxyselenolo[3,4-b]-thiophene (XXII) was the first described derivative of this system.

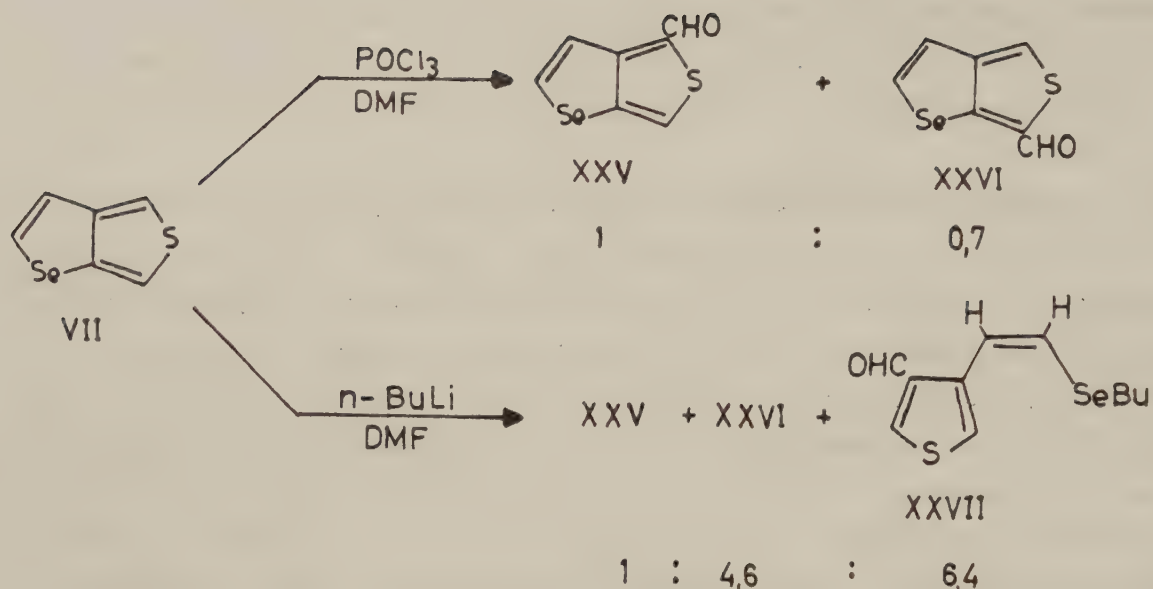
Similarly the selenophene ring in XXIII was also destroyed upon hydrolysis, although to a lesser extent, allowing isolation of the desired 2-carboxyselenolo[3,4-b]selenophene (F 9). Hence, the reaction sequence of Scheme IV could be accomplished, yielding the parent selenophene XII in 2.6 % yield based on the bischloro derivative XIX. Because of the low, over-all yield in this multi-step synthesis, other approaches to XII were also tried. Application of the, otherwise very useful, Dieckmann cyclization route proved unsuccessful - only resinification products were obtained in the reaction of n-butyllithium with 2-(4-bromo-3-selenienyl)-1,3-dioxolane and subsequent treatment with red selenium and methyl bromoacetate. Recently, Goldfarb et al.²³ reported an unexpected formation of 3-bromoselenolo[2,3-b]selenophene-5-carboxylic acid in their attempted preparation of selenolo[3,4-b]selenophene (XII) starting from 3,4-dibromoselenophene. This result was explained by a hindered halogen-lithium exchange and a preferable metalation in the 2-position of selenophene ring. Neither could selenolo[2,3-c]-thiophene (VII) be prepared by a Dieckmann cyclization route,⁸ thus indicating the difficulties encountered in attempts to carry out the ring-closure on the 3- and 4-positions of the thiophene or selenophene ring. Concerning these results, it is then not surprising that the above-mentioned analogous approach to selenolo[3,4-b]selenophene (XII) failed. Applying the route proposed by Litvinov et al.⁸ gave, however, XII in 44 % yield when starting from 4-methylseleno-3-selenophene aldehyde (XXIV) (cf. Scheme IV). Its methylseleno group was quaternized with methyl bromoacetate in toluene to give an intermediate selenonium salt (F 11), which was then cyclized to the ester XXIII. Hydrolysis and decarboxylation afforded selenolo[3,4-b]selenophene (XII), which appeared to be indefinitely stable when kept in a refrigerator and at least for a week at

room temperature in air. This behaviour is in marked contrast to the known instability of thieno[3,4-b]thiophene (III),³ but resembles rather the behaviour of selenolo[2,3-c]thiophene (VII),⁸ which like XII is also a stable, crystalline compound.

3.2. Electrophilic substitution and ring-opening reactions

Wynberg et al., who first synthesized thieno[3,4-b]thiophene (III),³ have also carried out some substitution reactions on it,⁵⁷ finding that both electrophilic attack and metalation take place at positions 4 and 6, in accordance with predictions based on quantum chemical calculations. (For a review of quantum chemical calculations and the reactivities of isomeric thiophenes, see Ref. 5 and references therein.) The reactions carried out by Wynberg et al.⁵⁷ on III were the Vilsmeier formylation, which gave a mixture of 4- and 6-formyl derivatives in a ratio of 70:30, and metalation with n-butyllithium, where a reversal of the product ratio (20:80) was observed. Although a selenium analogue of III, selenolo[2,3-c]thiophene (VII), has been synthesized,⁸ there are no reports in the literature concerning its reactivity. Therefore in Paper G, a study of the Vilsmeier formylation and metalation of VII was undertaken. The experimental conditions were the same as in the work of Wynberg et al.,⁵⁷ in order to enable comparison with the results obtained for thieno[3,4-b]thiophene (III).

Vilsmeier formylation of VII gave a mixture of 4- and 6-selenolo[2,3-c]thiophene aldehydes XXV and XXVI, in a ratio of 60:40. Metalation with n-butyllithium at -20°C, followed by formylation of the resulting organolithium compound changed this ratio to 18:82 and in addition gave XXVII, a product of ring-opening reaction. These results, summarized in Scheme V, are in very good agreement with those obtained for thieno[3,4-b]thiophene (III),⁵⁷ both regarding the preferential sites of electrophilic attack and the ratios of the products formed.



Scheme V

The reversal of product ratios on going from electrophilic substitution to metalation can be rationalized by the possible coordination of the lithium atom in the 6-position with either the adjacent sulfur or selenium atom. With the exception of the ring-opening reaction that gives XXVII, selenolo[2,3-c]-thiophene (VII) behaves very much like its sulfur analogue III both on electrophilic substitution and metalation. In view of the several ring-opening reactions of selenophenes discovered during the past few years (for review see Ref. 58 and references therein), the ring-opening of VII was not unexpected. According to the classification proposed by Gronowitz and Frejd,⁵⁸ the ring-opening of VII is of the RO II-type with the mechanism outlined in Scheme II in Paper G. This is the first reported case of cleavage between a selenium atom and a β -carbon of a thiophene ring. A similar ring-opening of selenolo[2,3-b]thiophene (V) has been reported, although its "trans" isomer VI is attacked by n -butyllithium in the normal way and does not undergo any ring-opening reaction. Obviously, this difference in the reactivity towards n -butyllithium between the "cis" and

"trans" systems V and VI is due to relative positions of the heteroatoms. Since it is known that ring strain increases the tendency for reaction of the RO II-type,⁵⁸ the steric ring inhibition should be more effective in compounds with "cis" configuration due to the vicinity of the heteroatoms. An assumption that the ring strain is a main factor responsible for the cleavage of the C-Se bond in the "cis" compounds, leads to the conclusion that the type of annelation present in selenolo[2,3-c]thiophene (VII) gives rise to a degree of ring strain closer to that in selenolo[2,3-b]thiophene (V) than in its "trans" isomer VI.

3.3 ¹H, ¹³C and ⁷⁷Se NMR spectra

The ¹H NMR spectra of thieno[3,4-b]thiophene (III),³ selenolo[2,3-c]thiophene (VII)⁸ and selenolo[3,4-b]selenophene (XII) (Paper F) are all first order with well separated signals for all four aromatic protons. As expected, the resonance of the only β-proton, H-3, occurs at the highest field and, as discussed in Chapter 2.3., the resonances of all the protons are shifted to lower field on going from III to VII and XII. The vicinal coupling between H-2 and H-3 also increases in the same series. Long-range spin-spin interactions between H-3 and H-6 separated by five bonds are observed in VII and XII, which facilitates differentiation between H-4 and H-6. In both VII and XII, H-6 is more shielded than H-4. The reversed assignment of these protons in III, proposed by Wynberg et al.,³ is probably due to the fact that the long-range coupling was not observed, and should now be revised.

¹H NMR spectroscopy is also helpful in determining the preferred form of the aldehydes XXV and XXVI (Paper G) and their sulfur analogues.⁵⁷ In both cases the aldehydic proton of the 4-substituted derivatives appears as a doublet, whereas that of the 6-substituted compounds as a sharp singlet. Since such coupling is known to be transmitted only along a regular zig-zag path, this indicates a preferential existence of the S-cis form in 4-aldehydes and the S-trans form in 6-aldehydes.

This is further corroborated by ^{77}Se spectra of XXIV and XXV, where an anomalously large upfield shift of the selenium atom in the 6-substituted aldehyde is observed, probably due to an attractive binding interaction between the carbonyl oxygen lone-pair and the selenium d-orbitals, as suggested by Gronowitz et al.⁵⁰

The ^{13}C NMR spectra of selenolo[2,3-c]thiophene (VII) and selenolo[3,4-b]selenophene (XII) are reported in Papers G and F, respectively, and the chemical shifts are given in the Table on page 18. Assignment of the signals was discussed in detail in Paper G. It was greatly facilitated by comparing the data for the derivatives of VII with different substitution patterns. There are no simple regularities in the ^{13}C spectra of VII and XII regarding the chemical shifts, such as in the spectra of the compounds with the [2,3-b]- or [3,2-b]-type of annelation. Absorption of C-3, the only β -carbon, occurs at intermediate field between absorptions of C-2, and C-4 and C-6. The absorptions of C-4 and C-6 lie very near each other, C-4 absorbing at higher field in VII and at lower in XII. There are, however, some regularities regarding coupling constants, the direct coupling $^1J_{\text{C3-H3}}$ always being the smallest, as was also the case for β -carbons in the [2,3-b] and [3,2-b] compounds. The direct couplings of α -carbons in both VII and XII decrease in the series $\text{C6} > \text{C4} > \text{C2}$.

In the Table on page 18 the ^{77}Se parameters of VII and XII are also included. As discussed in Chapter 2.4., the fusion of either a thiophene or a selenophene ring onto that of selenophene has a shielding effect on the selenium atom, in the [2,3-b]- and [3,2-b]-fused compounds the effect of a thiophene fusion is much greater. This difference is levelled out in compounds VII and XII, where the Se-1 atoms absorb at almost the same frequencies: 173.8 and 176.4 ppm upfield from selenophene, respectively. These selenium atoms are, in fact, the most shielded found in any heteroaromatic selenium compounds to date (cf. Figure 2) and fall into the ^{77}Se shift region of diaryl selenides.⁵⁹ On the other hand, as mentioned in Chapter 2.4., the absorption of Se-5 atom in XII at 126 ppm downfield from selenophene constitutes the downfield limit of

selenium-containing heterocycles (cf. Figure 2.2). This great shift difference of over 300 ppm was, in Paper F, attributed to an appreciable charge separation in XII, with Se-5 being the more positively charged of the two selenium atoms. This assumption was further substantiated by the fact that the resonance of Se-5 was very near to that of diphenyl selenoxide, which has partial positive charge. Recent results of PPP and CNDO/2 calculations on XII^{60,61} indicate a charge difference between Se-1 and Se-5 in the right direction, although of too small a magnitude to, alone, account for the observed shift difference in the ⁷⁷Se NMR spectrum of XII. Thus, it seems that the charge distribution in the molecule is insufficient to account for the observed shift difference and the effect must be due, in part at least, to other factors.

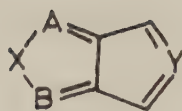
4. THE [3,4-c] -ANNELATED SYSTEMS

The last possible way of fusing two five-membered heterocyclic rings each containing one heteroatom, is a [3,4-c] -annellation. In the case of thiophene and/or selenophene, it results in the three [3,4-c] -fused compounds depicted in Scheme I: thieno[3,4-c]thiophene (IV), selenolo[3,4-c]thiophene (IX) and selenolo[3,4-c]selenophene (XIII). The only uncharged resonance contributors that can be written for these compounds contain a tetravalent sulfur or selenium atom in one of the rings, and for this reason they are frequently referred to as "nonclassical". The term "nonclassical" has been used by Cava et al.⁴ in relation to the possibility that, in some sulfur-containing species, the participation of d-orbitals may be important in the bonding. This concept of d-orbital bonding participation in sulfur heterocycles was initially proposed in 1939 by Schomaker and Pauling⁶² for the case of thiophene. The suggestion was made that an expansion of the sulfur octet could be a special factor in the stabilization of the thiophene molecule. Ten years later, this concept was developed in molecular orbital terms by Longuet-Higgins,⁶³ who demonstrated that the mixing of $3p_z$, $3d_{xz}$ and $3d_{yz}$ orbitals of sulfur would provide three pd^2 hybrid orbitals, two of which would be capable of π -overlap. This led to sulfur being treated as equivalent to a vinyl group in Hückel-type calculations on thiophene- and other sulfur-containing heterocycles.⁶⁴ Today, over 40 years after the original proposal of Schomaker and Pauling,⁶² the issue of d-orbital bonding participation in sulfur heterocycles is still not completely resolved. It has, however, stimulated numerous investigations of both theoretical and experimental nature and the concept has recently been reviewed by Reid.⁶⁵

Bicyclic 10π -electron heterocycles containing a "nonclassical" thiophene nucleus constitute a group of compounds especially suitable for studying this problem and are thus of considerable theoretical interest. A continuously growing amount of research in this field has also been reviewed several

times and the review articles dealing with the topic include "The Chemistry of Some Tetracovalent Condensed Thiophenes" by Cava,⁶⁶ "Nonclassical Condensed Thiophenes" by Cava and Lakshmikantham,⁴ "Heteropentalenes" by Potts,⁶⁷ and "Mesomeric Betaine Derivatives of Heteropentalenes" by Ramsden.⁶⁸ A brief look at these titles reveals that even the nomenclature of this class of compounds is still the subject of discussion, as is certainly the nature of sulfur bonding and the electronic structure.^{69,70} The current situation regarding this matter is possibly best characterized by two remarks, which are perhaps worth including here. As pointed out by Ramsden,⁶⁸ "there is no law of nature which requires that molecules be represented by purely covalent structures. The observation that without inclusion of d-orbitals the thieno[3,4-c]thiophenes can only be represented as mesomeric betaines is not sufficient justification, without other evidence, for invoking d-orbital participation". And a concise comment by Cava and Lakshmikantham:⁴ "further insight into this problem will be best gained not by polemics but by new experimental work".

Since the time this comment was made, there has been a lot of new experimental work in the field. Of the nine conceivable "nonclassical" condensed thiophenes represented by structure XXVIII (where A and B = CR or N, X = O, S or NR and Y = S), eight have been synthesized to date as their highly phenylated derivatives, and details of their chemistry have been studied. Extension of the general formula XXVIII to selenium, i.e. A and B = CR or N, X = O, S, Se or NR and Y = S or Se, provides a further 12 structural possibilities, of which only selenolo[3,4-c]thiophenes and selenolo[3,4-c]-selenophenes have been investigated.

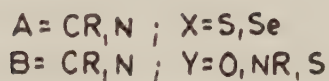
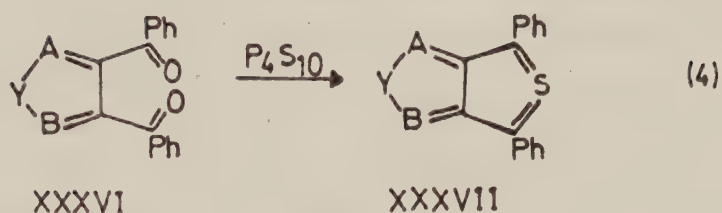


XXVIII

Parent heterocycle	No	A	X	B	Y	Ref.
Thieno [3,4-c] furan	XXIX	CH	O	CH	S	71
Thieno [3,4-c] thiophene	IV	CH	S	CH	S	4,66-70,80
Thieno [3,4-c] pyrrole	XXX	CH	NR	CH	S	71,72
Thieno [3,4-c] isothiazole	XXXI	CH	S	N	S	73,74
Thieno [3,4-c] pyrazole	XXXII	CH	NR	N	S	75,76
Thieno [3,4-c] [1,2,5] oxadiazole	XXXIII	N	O	N	S	77
Thieno [3,4-c] [1,2,5] thiadiazole	XXXIV	N	S	N	S	78
Thieno [3,4-c] [1,2,3] triazole	XXXV	N	NR	N	S	67,79
Selenolo [3,4-c] thiophene	IX	CH	Se	CH	S	9,J
Selenolo [3,4-c] selenophene	XIII	CH	Se	CH	Se	H,J

4.1. Synthesis

There are few synthetic routes leading to a nonclassical sulfur or selenium heterocycles. The most important ones are summarized in Scheme VI. Route (1) utilizes a Pummerer-type dehydration of a suitable sulfoxide or selenoxide, as originally proposed by Cava et al. (cf. Ref. 4 and references therein). In fact, the first reported derivative of thieno [3,4-c] thiophene (IV), the 1,3-dimethyl-substituted compound,⁸⁰ as well as the third "classical" thiophene, thieno [3,4-b] thiophene (III),³ were prepared by this route. Formation of some condensed thiophenes by a base-catalyzed sulfoxide dehydration, according to route (2), was also reported by Cava et al.,²¹ as well as the base-catalyzed reductive debromination of a selenium dibromide,^{9,82} according to route (3). The cyclothiation of the vic-dibenzoyl heterocycles (XXXVI) to the corresponding bicyclic thiophene derivatives XXXVII using phosphorus pentasulfide, according to route (4), is now an established way to the



Scheme VI

nonclassical condensed thiophenes. In fact, all of the stable, fully phenylated derivatives of the general structure XXXVII (A and B = CPh, N) reported to date, which comprises derivatives of IV and XXX-XXXV, have been prepared by this procedure. An attempt to synthesize the tetraphenyl derivative of thieno-[3,4-c]furan (XXIX) by the reaction of 3,4-dibenzoyl-2,5-diphenylfuran (XXXVI, A = B = CPh, Y = O) with phosphorus pentasulfide in pyridine led to the exchange of oxygen in the furan ring by sulfur, tetraphenylthieno[3,4-c]thiophene being isolated in 96 % yield.⁷¹ The unstable tetraphenylthieno[3,4-c]furan has instead been prepared according to route (1), by the dehydration of its dihydro sulfoxide with acetic anhydride, and evidence for its transient existence has been provided by in situ trapping.⁷¹

If the reaction of 3,4-dibenzoyl-2,5-diphenylfuran or -thiophene with phosphorus pentasulfide was carried out in refluxing xylene, the product isolated was not, however, the anticipated thiophene XXXVII (A = B = CPh, Y = S), but rather

a mixture of its dihydro derivatives, as reported by Cava et al.^{71,83} On the contrary, in the recent review article by Potts, this reaction is claimed to give directly the nonclassical tetraphenylthieno[3,4-c]thiophene (cf. Ref. 67, p. 324), as was the case with the P_4S_{10} -pyridine reagent.^{71,72} Clearly the transformation of XXXVI into XXXVII by phosphorus pentasulfide is critically dependent on the reaction conditions. The first reported example of this general synthetic route was the preparation of 2,5-diphenylthieno[3,4-c][1,2,5]thiadiazole (XXXVII, A = B = N, Y = S), from the corresponding dibenzoyl precursor.⁷⁸ Although phosphorus pentasulfide in dioxane was used in this reaction, today, pyridine appears to be a solvent of choice. Since the formation of the nonclassical thiophene systems can also be effected by P_4S_{10} treatment in such solvents as toluene,⁷¹ xylene^{67,71} and dioxane,⁷⁸ the basic nature of pyridine in the reaction is probably not significant. Its expedient use is most likely due to the advantages offered in the work-up procedure.

As mentioned above, attempts to prepare tetraphenylthieno[3,4-c]furan by ring-closure of the 3,4-dibenzoylfuran XXXVI (A = B = CPh, Y = O) with phosphorus pentasulfide led to the exchange of oxygen by sulfur and isolation of tetraphenylthieno[3,4-c]thiophene in high yield.⁷¹ A similar exchange was also reported to occur by Potts on treatment of the 3,4-dibenzoyl-1,2,5-oxadiazole (XXXVI, A = B = N, Y = O) with P_4S_{10} in xylene as well as in pyridine, diphenylthieno[3,4-c][1,2,5]-thiadiazole (XXXVII, A = B = N, Y = S) being isolated in 65 % yield (cf. Ref. 67, p. 330). On the contrary, Tsuge et al.⁷⁷ have reported the above reaction to give the desired diphenylthieno[3,4-c][1,2,5]oxadiazole (XXXVII, A = B = N, Y = O) in 30 % yield. Since the reported yields for other phenylated heterocycles (IV, XXX-XXXII, XXXIV) formed in this reaction vary between 60 % and 96 %, the low yield reported by Tsuge et al.⁷⁷ might be due to the concurrent formation of the unobserved thienothiadiazole, but might also be due to the low stability of the thienooxadiazole system under the reaction conditions.

In conclusion it can be said that the reaction of P_4S_{10}

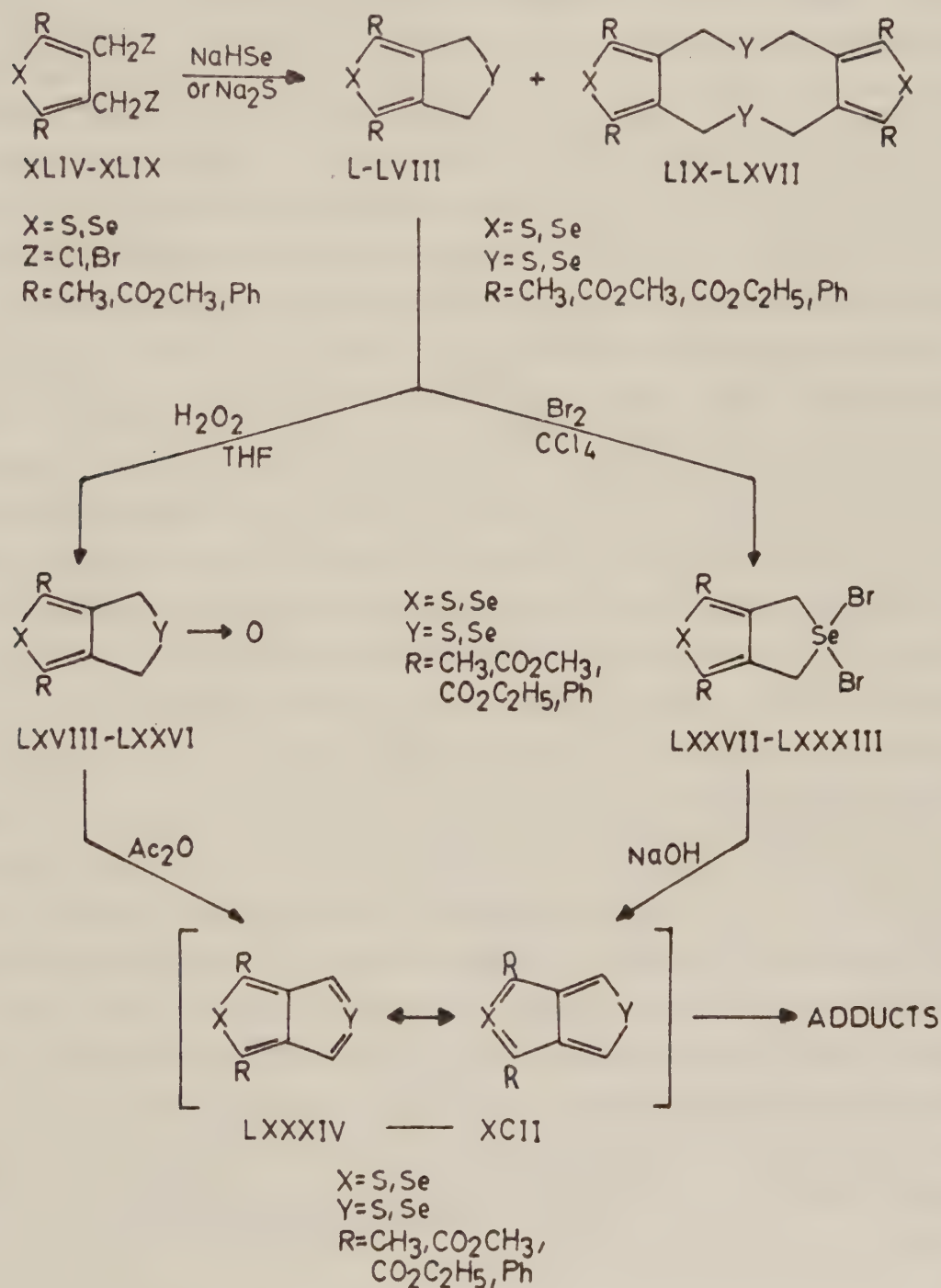
Extrusion of phenylisocyanate from the adduct XL leads to the thiophene diester XLII, or similarly to 3,4-dibenzoyl-2,5-diphenylthiophene (XXXVI, A = B = CPh, Y = S) if DMAD is replaced by dibenzoylacetylene. In contrast, the adduct XLI (X = Se) eliminates selenium to give the pyridone diester XLIII and not the required selenophene derivative.

In another attempt to extend the approach of route (4) to selenium heterocycles, the reaction of phosphorus pentaselenide with 1,4-diketones was investigated in Paper K and will be discussed in Section 4.3. Approaches to derivatives of the selenolo[3,4-c]selenophene system (XIII) along routes (1) and (3) were reported in a preliminary communication (Paper H), and full details of this work, as well as of the work on the mixed sulfur-selenium system IX are given in Paper J. A brief summary of these results is attempted in the following sections.

4.2. 1,3-Disubstituted selenolo[3,4-c]selenophenes

As mentioned above, the first reported derivatives of thieno-[3,4-c]thiophene (IV), the 1,3-dimethyl- and 1,3-dicarbomethoxy-substituted compounds, were synthesized by route (1) in Scheme VI.^{4,80} Quite naturally, in Paper H, this approach was also chosen for the preparation of the corresponding derivatives of selenolo[3,4-c]selenophene (XIII), and in Paper J it was extended to the 1,3-diphenyl-substituted derivative. The required starting materials, 3,4-bishalomethylselenophenes XLIV-XLVI (X = Se, R = CH₃, CO₂CH₃, Ph in Scheme VIII), were prepared according to the synthetic routes outlined in Schemes 2 and 6 in Paper J. In all three cases, the ring-closure reactions with ethanolic sodium hydrogen selenide gave mixtures of the required dihydroselenophenes L-LII, their dimers LIX-LXI and even higher oligomers, from which the monomers could be separated by steam distillation or fractional crystallization. Periodate oxidation according to Cinquini et al.,⁸⁷ or, preferably, oxidation with hydrogen peroxide in tetrahydrofuran, afforded the selenoxides LXVIII-LXX, and bromination with bromine in carbon tetrachloride gave the dibromides LXXVII-LXXIX in very good yields. These

compounds served as starting materials for the generation of the nonclassical selenolo[3,4-c]selenophenes LXXXIV-LXXXVI ($X = Y = \text{Se}$, $R = \text{CH}_3$, $\text{CO}_2\text{C}_2\text{H}_5$ or Ph); the selenoxides according to route (1) or (2) and the dibromides according to route (3) in Scheme VI. All of the above transformations are schematically depicted in Scheme VIII, which will be referred to also in Section 4.4 on the mixed sulfur-selenium systems.



Scheme VIII

When a solution of the selenoxide LXVIII ($X = Y = \text{Se}$, $R = \text{CH}_3$) in acetic anhydride was heated to reflux under nitrogen, an intense red-violet, fluorescent colour developed rapidly. This colour was attributed to the presence of the nonclassical selenolo[3,4-c]selenophene LXXXIV in the solution, and it remained unchanged for an additional 3 hours of refluxing. Similar results were obtained with the diphenyl-substituted selenoxide LXX ($X = Y = \text{Se}$, $R = \text{Ph}$). However, the dicarbethoxy-substituted selenoxide LXIX ($X = Y = \text{Se}$, $R = \text{CO}_2\text{C}_2\text{H}_5$) could not be isolated in the pure state since the hydrogen peroxide oxidation of LI led directly to the development of the violet colour of the THF solution, which remained for over 5 hours. On attempts to isolate these violet products, mixtures of dihydroselenophenes L-LII, their dimers LIX-LXI and higher oligomers were obtained. In the case of the dicarbethoxy-substituted product it was, however, possible to record the UV spectrum ($\lambda_{\text{max}} = 563 \text{ nm}$ in hexane) and the NMR spectrum in C_6D_6 , which showed a single peak for the aromatic protons at $\delta 10.04 \text{ ppm}$, besides the carbethoxy groups.

The dibromides LXXVII-LXXIX were decomposed within a few minutes when stirred with 40 % sodium hydroxide solution at 0°C under nitrogen. When the resulting milky emulsions were stirred with hexane or benzene, the selenolo[3,4-c]selenophenes LXXXIV-LXXXVI were released into the organic phase, as followed by the appearance of a deep violet colour of the organic layer. Upon attempting isolation of these violet products, mixtures of selenides, their dimers and some polymeric material, similar to those isolated on dehydration of selenoxides, were obtained. If the duration of the colours observed can be taken as a measure of the stability of the differently substituted nonclassical selenophenes, then the order of relative stabilities would be: LXXXV ($R = \text{CO}_2\text{C}_2\text{H}_5$) > LXXXVI ($R = \text{Ph}$) > LXXXIV ($R = \text{CH}_3$), indicating a stabilizing effect of electron-withdrawing groups on the selenolo[3,4-c]selenophene system (XIII). On the other hand, the steric interference of the phenyl groups in tetraphenylthieno[3,4-c]thiophene was found to be the main factor responsible for its stability^{69,70} and this effect might also play a role in the case of LXXXVI.

As mentioned above, selenoloselenophenes LXXXIV-LXXXVI are too unstable to be isolated in the pure state, but they can be trapped with various dipolarophiles in 1,3-dipolar cycloaddition reactions. As pointed out by Ramsden,⁶⁸ such reactions are mainly governed by two factors: (i) the energy and symmetry of the HOMO of the heteropentalene and (ii) the thermodynamic stability of the cycloadduct. In the case of nonclassical condensed thiophenes,⁴ dienophile addition takes place at the ring of highest electron density, i.e. as expected for an aromatic, delocalized system.

If the dehydration of selenoxides LXVIII-LXX was carried out in the presence of N-phenylmaleimide (NPM) or if NPM was added to the violet solutions formed, the reactions were normally completed within a few minutes, as indicated by the disappearance of the violet colours. In all three cases a few crystals of the adducts were isolated, the compositions of which were confirmed by their mass spectra. Unfortunately, since the NMR spectra could not be recorded, the structure assignments are, as yet, uncertain as to the site of dienophile addition, as well as to the endo/exo conformation of the adducts. Most probably, reaction with NPM takes the same course for selenolo[3,4-c]selenophenes as for the corresponding sulfur analogs,⁴ i.e. the addition takes place at the ring of highest electron density, and both endo and exo adducts are generated, with the exo conformation predominating.

Other dienophile reagents than N-phenylmaleimide can also be used to trap the unstable selenolo[3,4-c]selenophene system and, in Paper J, some such reactions were described. Reaction with dimethylacetylenedicarboxylate led to the tetracarbomethoxy naphthalene (J 24) which, being a product of the double-sided addition and aromatization, prevented the determination of the primary sites of addition. Tetracyanoethylene did not give the expected products of dienophile addition but rather the selenonium dicyanomethylides (J 25) and (J 26). Adducts could not even be obtained with 4-phenyl-1,2,4-triazoline-3,5-dione, the most powerful dienophile so far reported.^{88,89}

4.3. . 1,3,4,6-Tetrasubstituted selenolo [3,4-c] selenophenes and -thiophenes

Since the only stable derivative of the thieno [3,4-c] thiophene system (IV) prepared to date is a tetraphenyl-substituted compound,⁷¹ an attempt to synthesize its selenium analog, 1,3,4,6-tetraphenylselenolo [3,4-c] selenophene was made in Paper K. The thiophene (K II) was prepared in one step in 96 % yield by treatment of tetrabenzoylthane (K I) with phosphorus pentasulfide in pyridine,⁷¹ and a similar approach to the selenophene, i.e. the reaction of tetrabenzoylthane with phosphorus pentaselenide, was chosen. However, the reaction of the commercially available P_2Se_5 , as well as of P_2Se_5 prepared according to Zingaro et al.,⁹⁰ with tetrabenzoylthane in various solvents, did not afford any selenium-containing products. Neither could the ring-closure of two other 1,4-diphenyl-1,4-dicarbonyl compounds (K V) be effected. First a slight modification of the procedure of Zingaro et al.,⁹⁰ in which red amorphous selenium was used instead of the grey form, rendered phosphorus pentaselenide of such a quality, that the ring-closure of tetrabenzoylthane, as well as of other 1,4-diketones, could be accomplished. In contrast to the direct generation of the nonclassical tetraphenylthiophene (K II) on treatment of tetrabenzoylthane with P_4S_{10} in pyridine,⁷¹ no formation of the corresponding tetraphenylselenolo [3,4-c]-selenophene could be observed. Instead, a mixture of cis- and trans-dihydroselenophenes (K IV) was formed in 40 % yield. Oxidation gave a selenoxide (K VII), which decomposed on warming, with the development of a deep blue-green colour, possibly indicating the formation of the nonclassical selenolo-[3,4-c]selenophene system. Attempts to generate this system by warming a solution of the selenoxide in acetic anhydride have not yet been successful.

In order to further investigate the above double-sided ring-closure reaction of the tetraone skeleton, and at the same time to increase the possibility for delocalization in the desired system, reactions of the tetraketones (J 61) and (J 62) with P_4S_{10} and P_2Se_5 in pyridine were attempted (Paper J). These

structures were designed by connecting the carbonyl carbons of the tetraketone skeleton through five- or seven-membered rings, which was hoped to stabilize the nonclassical compounds (J 63) - (J 66). Unfortunately, no such compounds could be detected among the reaction products.

Recently, Lepage et al.⁹¹ have observed the formation of benzo[c]thiophene derivatives on treatment of some o-dibenzyl-benzenes with sulfur. Similar reaction of 3,4-dibenzyl-substituted thiophenes or selenophenes would thus give the nonclassical thienothiophenes or selenolothiophenes, respectively (cf. Scheme 7 in Paper J). The required starting compounds (J 51) - (J 53), were prepared from the 3,4-bishalomethyl thiophenes or selenophenes by the Friedel-Crafts reaction with benzene, but none of the expected nonclassical systems (J 54) - (J 56) was formed on the reaction with sulfur.

4.4. 1,3- and 4,6-disubstituted selenolo[3,4-c]thiophenes

The synthetic approaches to the derivatives of selenolo[3,4-c]-thiophene (IX), described in the second part of Paper J, mainly followed routes (1) and (3) of Scheme VI. The required starting dihydroselenolothiophenes LIII-LV (X = S, Y = Se, R = CH₃, CO₂C₂H₅, Ph in Scheme VIII) and LVII-LVIII (X = Se, Y = S, R = CH₃, CO₂CH₃), were prepared by ring-closure of the corresponding 3,4-bishalomethylthiophenes with sodium hydrogen selenide or by ring-closure of 3,4-bishalomethylselenophenes with sodium sulfide, respectively. The synthetic sequences leading to the nonclassical selenolothiophenes LXXXVII-LXXXIX and XCI-XCII, analogous to those described in Section 4.2 for the corresponding selenolo[3,4-c]selenophene derivatives, are outlined in Scheme VIII and in somewhat greater detail in Scheme 10 in Paper J.

During the time this work was in progress, Saris and Cava⁹ reported the generation and trapping of 1,3-dimethyl- and 1,3-dicarbomethoxyselenolo[3,4-c]thiophenes LXXXIV and XC. With the exception that the ring-closure reaction of the thiophene XLVIII (X = S, R = CO₂CH₃, Z = Br) was brought

about by aqueous NaHSe in dioxane, which gave the dicarbomethoxy derivative LVI (dicarbethoxy compound LV was described in Paper J), most of the results obtained by these authors and in the present work were in good agreement (see Ref. 9 and Paper J).

In another attempt to prepare a derivative of the selenolo-[3,4-c]thiophene system, prompted by a report of Cignarella and Cordella^{92,93} on an alkali-induced rearrangement of 1,4-dicarbomethoxy-2,3-benzodithiane (J 98) to a benzo[c]thiophene (J 99), a similar reaction of selenolodithianes (J 100) and (J 101) was tried. However, reflux with methanolic sodium methoxide resulted in a quantitative recovery of the dimethyl-substituted selenolodithiane (J 100) and decomposition of the dicarbomethoxy-substituted compound (J 101), no nonclassical selenolothiophenes being observed. Similar results were obtained with the analogous thienodithianes, which would lead to the known derivatives of the nonclassical thieno[3,4-c]thiophene (IV).⁸⁰ Since the rearrangement of the benzodithiane (J 98) to a benzo[c]thiophene derivative (J 99) was shown to be favoured by the inductive effect of the carbomethoxy groups in the 1,4-positions, an attempt to synthesize the corresponding selenolodithianes (J 108) and J 109) along the route outlined in Scheme 12 in Paper J, was made. Owing to the difficulties in the bromination α to the carbethoxy groups of (J 104) and (J 105), this approach was not successful.

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6. REFERENCES

1. A. Biedermann and P. Jacobson, Chem. Ber. 19, 2444 (1886)
2. F. Challenger and J.B. Harrison,
J. Inst. Petrol. Techn. 21, 135 (1935)
3. J. Wynberg and D.J. Zwanenburg, Tetrahedron Letters
1967, 761
4. M.P. Cava and M.V. Lakshmikantham,
Acc. Chem. Res. 8, 139 (1975)
5. V.P. Litvinov and Ya.L. Goldfarb,
Advan. Heterocycl. Chem. 19, 123 (1976)
6. A. Bugge, Acta Chem. Scand. 23, 1823 (1969)
7. Ya.L. Goldfarb, V.P. Litvinov and S.A. Ozolin,
Izv. Akad. Nauk SSSR, Ser. Khim. 1968, 1419
8. V.P. Litvinov, A.N. Sukiasyan, Ya.L. Goldfarb and
L.V. Bogacheva, Izv. Akad. Nauk SSSR, Ser. Khim. 1971, 1592
9. L.E. Saris and M.P. Cava, Heterocycles 6, 1349 (1977)
10. V.P. Litvinov, Ya.L. Goldfarb, V.S. Bogdanov,
I.P. Konjaeva and A.N. Sukiasyan, J. prakt. Chem. 315,
850 (1973)
11. V.A. Briscoe, J.B. Peel and P.L. Robinson,
J. Chem. Soc. 1928, 2628
12. S. Umezawa, Bull. Chem. Soc. Japan 14, 363 (1939)
13. S. Gronowitz and B. Persson, Acta Chem. Scand.
21, 812 (1967)
14. Ya.L. Goldfarb, S.A. Ozolin and V.P. Litvinov,
Khim. Geterots. Soedin. 3, 935 (1967)
15. Ya.L. Goldfarb, V.P. Litvinov and S.A. Ozolin,
Izv. Akad. Nauk SSSR, Ser. Khim. 1965, 510
16. B. Tamamushi, H. Akiyama and S. Umezawa,
Bull. Chem. Soc. Japan 14, 318 (1939)
17. S. Gronowitz, T. Frejd and A.-B. Hörnfeldt,
Chemica Scripta 5, 236 (1974)
18. H. Tominaga, G. Hazato and H. Oshima,
J. Chem. Soc. Japan 63, 1291 (1943)
19. A.C. Villa, M. Nardelli and C. Palmieri,
Acta Crystallogr., Sect. B 25, 1374 (1969)

20. N.N. Magdesieva, *Advan. Heterocycl. Chem.* 12, 1 (1970)
21. N.N. Magdesieva and N.S. Zefirov, *Organic Selenium Compounds: Their Chemistry and Biology* (ed. D.L. Klayman and W.H.H. Günther), p. 427, Wiley Interscience, New York 1973
22. B. Capron and C. Paulmier, *C.R. Acad. Sci., Ser. C* 279, 947 (1974)
23. Ya.L. Goldfarb, V.P. Litvinov and I.P. Konjaeva, *Khim. Geterots. Soedin.* 1979, 1072
24. S.W. Schneller and J.D. Petru, *Synth. Commun.* 4, 29 (1974)
25. C.E. Redemann, R.N. Icke and G.A. Alles, *Org. Synth. Coll. Vol. III*, 763 (1955)
26. L. Henriksen, University of Copenhagen, private communication. The gift of carbon diselenide by Dr. Henriksen is gratefully acknowledged
27. L. Henriksen, *Int. J. Sulfur Chem.* 8, 389 (1973)
28. S. Gronowitz, T. Frejd, A. Moberg-Ogard and L. Trege, *J. Heterocycl. Chem.* 13, 1319 (1976)
29. V.P. Litvinov, Ya.L. Goldfarb and I.P. Konjaeva, *Izv. Akad. Nauk SSSR, Ser. Khim.* 1979, 372
30. G. Marino, *Advan. Heterocycl. Chem.* 13, 235 (1971)
31. A. Bugge, *Chemica Scripta* 2, 137 (1972)
32. S. Gronowitz, I. Johnson and A. Bugge, *Acta Chem. Scand.* B30, 417 (1976)
33. A. Bugge, *Chemica Scripta* 3, 190 (1973)
34. C.G. Swain and E.C. Lupton, *J. Am. Chem. Soc.* 90, 4328 (1968)
35. N.C. Cutress, T.B. Grindley, A.R. Katritzky, M.V. Sinnott and R.D. Topsom, *J. Chem. Soc. Perkin Trans. 2*, 1972, 2255
36. For a comprehensive review of the "state of the art" in this field, see "NMR and the Periodic Table", Ed. by R.K. Harris and B.E. Mann, Academic Press 1978, and leading references therein.
37. W. McFarlane and R.J. Wood, *J. Chem. Soc. Dalton* 1972, 1397
38. S. Gronowitz, I. Johnson and A.-B. Hörnfeldt, *Chemica Scripta* 3, 94 (1973)
39. H.J. Reich and J.E. Trend, *J. Chem. Soc., Chem. Commun.* 1976, 310

40. M. Lardon in "Organic Selenium Compounds: Their Chemistry and Biology", Ed. by D.L. Klayman and W.H.H. Gunther, Wiley-Interscience, New York 1973, p. 933
41. V. Svanholm in "Organic Selenium Compounds: Their Chemistry and Biology", Ed. by D.L. Klayman and W.H.H. Gunther, Wiley-Interscience, New York 1973, p. 903
42. J.D. Odom, W.H. Dawson and P.D. Ellis, J. Am. Chem. Soc. 101, 5815 (1979)
43. W.H. Dawson and J.D. Odom, J. Am. Chem. Soc. 99, 8352 (1977)
44. W.-H. Pan and J.P. Fackler, J. Am. Chem. Soc. 100, 5783 (1978)
45. O.A. Gansow, W.D. Vernon and J.J. Dechter, J. Magn. Res. 32, 19 (1978)
46. W. Koch, O. Lutz and A. Nolle, Z. Naturforsch. A 33, 1025 (1978)
47. H. Kohlshorn and H. Meier, J. Chem. Res. (S), 1977, 338
48. M. Baiwir, G. Llabres, J.-L. Piette and L. Christiaens, Org. Magn. Res. 1980, in press
A manuscript of this paper obtained from the authors prior to publication is gratefully acknowledged.
49. G.A. Kalabin, D.F. Kushnarev, V.M. Bzesovsky and G.A. Tschmutova, Org. Magn. Res. 12, 598 (1979)
50. S. Gronowitz, I. Johnson and A.-B. Hörnfeldt, Chemica Scripta 8, 8 (1975)
51. A. Konar, unpublished results
52. L. Christiaens, J.-L. Piette, L. Laitem, M. Baiwir, J. Denoel and G. Llabres, Org. Magn. Res. 8, 354 (1976)
53. R. Gleiter and J. Spanget-Larsen, Topics in Current Chemistry 86, 139 (1979)
54. T. Koopmans, Physica 1, 104 (1934)
55. P.A. Clark, R. Gleiter and E. Heilbronner, Tetrahedron 29, 3085 (1973)
56. V.P. Litvinov and G. Fraenkel, Izv. Akad. Nauk SSSR, Ser. Khim. 1968, 1828
57. H. Wynberg and J. Feijen, Rec. Trav. Chim. Pays-Bas 89, 77 (1970)

58. S. Gronowitz and T. Frejd,
Khim. Geterotsikl. Soedin. 1978, 435
59. S. Gronowitz, A. Konar and A.-B. Hörnfeldt,
Org. Magn. Res. 9, 213 (1977)
60. R. Gleiter, private communication
61. M. Baiwir, private communication
62. V. Schomaker and L. Pauling,
J. Am. Chem. Soc. 61, 1769 (1939)
63. H.C. Longuet-Higgins, Trans. Faraday Soc. 45, 173 (1949)
64. A. Streitwieser, "Molecular Orbital Theory for Organic Chemists", Wiley, New York, N.Y., 1961
65. D.H. Reid in "Organic Compounds of Sulphur, Selenium and Tellurium" (Specialist Periodical Reports), Vol. 3, p. 392, The Chemical Society, London 1975.
66. M.P. Cava, Int. J. Sulfur Chem. Part C, 7, 55 (1972)
67. K.T. Potts in "Special Topics in Heterocyclic Chemistry", Ed. by A. Weissberger and E.C. Taylor, Wiley, New York, N.Y., 1977, p. 317
68. C.A. Ramsden, Tetrahedron 33, 3203 (1977)
69. C. Müller, A. Schweig, M.P. Cava and M.V. Lakshmikantham, J. Am. Chem. Soc. 98, 7187 (1976)
70. R. Gleiter, R. Bartetzko, G. Brähler and H. Bock, J. Org. Chem. 43, 3893 (1978)
71. M.P. Cava, M.A. Sprecker and W.R. Hall, J. Am. Chem. Soc. 96, 1817 (1974)
72. K.T. Potts and D. McKeough, J. Am. Chem. Soc. 96, 4268 (1974)
73. H. Gotthardt and F. Reiter, Tetrahedron Lett. 1976, 2163
74. H. Gotthardt and F. Reiter, Chem. Ber. 112, 266 (1979)
75. K.T. Potts and D. McKeough, J. Am. Chem. Soc. 96, 4276 (1974)
76. K.T. Potts, H.P. Youzwak and S.J. Zurawel, Jr., J. Org. Chem. 45, 90 (1980)
77. O. Tsuge, T. Takata and M. Noguchi, Heterocycles 6, 1173 (1977)
78. J.D. Bower and R.H. Schlessinger, J. Am. Chem. Soc. 91, 6891 (1969)
79. K.T. Potts and J. Considine, unpublished results
80. M.P. Cava and N.M. Pollack, J. Am. Chem. Soc. 89, 3639 (1967)

81. C.J. Horner, L.E. Saris, M.V. Lakshmikantham and M.P. Cava, Tetrahedron Lett. 1976, 2581
82. L.E. Saris and M.P. Cava, J. Am. Chem. Soc. 98, 867 (1976)
83. M.P. Cava, M. Behforouz, G.E.M. Husbands and M. Srinivasan, J. Am. Chem. Soc. 95, 2561 (1973)
84. W.D. Ollis and C.A. Ramsden, Advan. Heterocycl. Chem. 19, 1 (1976)
85. M.P. Cava and L.E. Saris, J. Chem. Soc., Chem. Commun. 1975, 617
86. K.T. Potts, F. Huang and R.K. Khattak, J. Org. Chem. 42, 1644 (1977)
87. M. Cinquini, S. Colonna and R. Giovini, Chem. and Ind. 1969, 1737
88. J. Sauer, Angew. Chem. 79, 76 (1967)
89. A.G. Williams and G.B. Butler, J. Org. Chem. 45, 1232 (1980)
90. M.V. Kudchadker, R.A. Zingaro and K.J. Irgolic, Can. J. Chem. 46, 1415 (1968)
91. L. Lepage and Y. Lepage, J. Heterocycl. Chem. 15, 1185 (1978)
92. G. Cignarella and G. Cordella, Tetrahedron Lett. 1973, 1871
93. G. Cignarella and G. Cordella, Gazz. Chim. Ital. 104, 455 (1974)

Paper A

On the Reaction between Acetylene and Selenium.

On the Reaction between Acetylene and Selenium

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Abstract

On the reaction between acetylene and selenium. Gronowitz, S., Konar, A.; Hörnfeldt, A.-B. (Division of Organic Chemistry 1, Chemical Center, University of Lund, P.O. Box 740, S-220 07 Lund, Sweden).

Chemica Scripta (Sweden) 1976, 10 (4), 159-164.

Selenolo[3,2-b]selenophene (I) and selenolo[2,3-b]selenophene (II) have been synthesized starting from lithium derivatives of 2-(3-bromo-2-selenienyl)-1,3-dioxolane and 2-(3-selenienyl)-1,3-dioxolane, respectively, by reaction with selenium and methyl chloroacetate followed by Dieckmann cyclization. Only I was detected among the products of the reaction between selenium and acetylene. In addition, about 30 other compounds were identified, for example 2- and 3-alkylselenophenes, 2- and 3-alkylselenoselenophenes, biselenienyls, benzo[b]selenophene, and also tricyclic-fused systems. An interesting compound, 2-methyl-1,3-diselenacyclopentene-4, was also isolated. The syntheses of some of the above-mentioned products are described.

Introduction

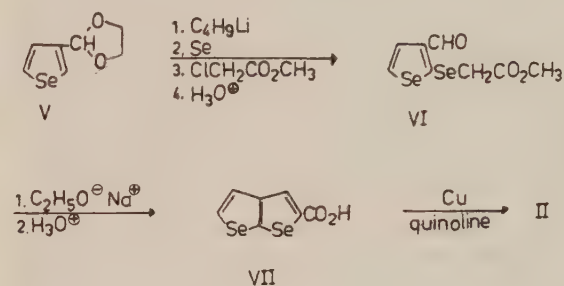
During recent years this laboratory has paid great interest to different types of selenophene derivatives for studies of ring-opening reactions [1], ^1H , ^{13}C [2, 3], and ^{77}Se [4] NMR parameters, utility of azides in organic synthesis [5], and the tautomeric properties of hydroxyselenophenes [6]. For these purposes we have prepared selenophene in a fairly large scale by reacting acetylene with selenium in a special tube oven. The details for this procedure will be published elsewhere [7]. However, in this reaction considerable amounts of higher-boiling products are also formed, and in this paper a detailed analysis of the product distribution is presented.

In previous work on the reaction between acetylene and selenium some higher-boiling products have been isolated. Mazza and Solazzo [8] have described benzoselenophene and Briscoe and co-workers [9] observed a sky-blue liquid. Umezawa examined the composition of the higher-boiling fraction of the selenophene synthesis and claimed that the major by-product, with m.p. 123-124.5°C, was selenolo[3,4-b]selenophene (III) [10]. The structure determination was mainly based on dipole moment measurements. However, by a combination of mass spectroscopy, ^{13}C and ^{77}Se NMR, and dipole moment measurements it was demonstrated by us that the substance, obtained in the same way as by Umezawa, was in fact selenolo[3,2-b]selenophene (I) [11]. In order to obtain an unambiguous evidence for the structures, selenolo[3,2-b]selenophene I and selenolo[2,3-b]selenophene (II) have now

been synthesized. Work on the synthesis of the third classical selenophene III, as well as the non-classical system IV, is in progress.

Results and Discussion

The synthetic route to selenolo[2,3-b]selenophene(II), as outlined in Scheme 1, is analogous to previous preparations in the thieno- and selenolothiophene series [12, 13].



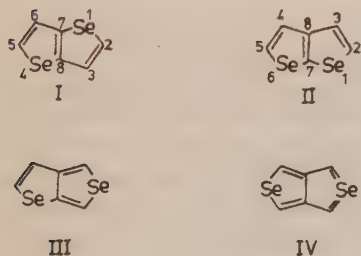
Scheme 1

2-(3-Selenienyl)-1,3-dioxolane (V) was metallated by butyllithium in the 2-position, and reacted with red, amorphous selenium. The intermediate selenienylselenolithium derivative was reacted with methyl chloroacetate and hydrolysed to give methyl (3-formyl-2-selenienylseleno)acetate (VI), which, without isolation, was cyclized with ethanolic sodium ethoxide solution to give 2-carboxyselenolo[2,3-b]selenophene (VII). Kvitko et al. [14] obtained a phenyl derivative of an analogous selenolo[2,3-b]-furan system by acidic cyclization of a corresponding (3-formyl-2-furylseleno)acetic acid. Because this reaction yielded directly the selenolo[2,3-b]furan system and not the acid, an attempt was made to cyclize the acetate VI with acetic anhydride and sodium acetate. The only reaction product besides the starting material was 3-formylselenophene, as neither acid VII nor the selenophene II was found. Decarboxylation of VII with copper in quinoline gave the selenophene II.

Also selenophene I was prepared in a similar way, starting from 2-(3-bromo-2-selenienyl)-1,3-dioxolane (VIII) via 2-carboxyselenolo[3,2-b]selenophene (IX).

IX showed the same melting point and spectroscopic data as those for the compound obtained by metallation and subsequent carbonation of the *trans*-selenophene formed during the selenophene preparation (see the Experimental part). Selenolo[3,2-b]selenophene (I), also had spectroscopic data and melting point in accordance with the *trans*-selenophene mentioned above.

The structure of II was confirmed by its ^1H , ^{13}C , and ^{77}Se NMR spectra, as well as by its mass spectrum. The ^1H NMR spectrum is of AA'BB' type, similar to that observed for thieno[2,3-b]-thiophene [15], with resonances of α - and β -protons occurring at



$\delta = 8.14$ and $\delta = 7.56$, respectively, i.e. at lower field than for thieno[2,3-*b*]thiophene. This is in accordance with previous investigations on selenophenes and thiophenes, where a stronger shielding in thiophenes is attributed to a more effective lone-pair conjugation of sulphur than of selenium [16]. The vicinal coupling between the α - and β -protons is larger than the corresponding coupling in thieno[2,3-*b*]thiophene, also in agreement with observations that selenophene couplings are larger than the corresponding thiophene couplings [2]. The long-range coupling constant between the α -protons equals 1.20 Hz, the same value as for thieno[2,3-*b*]thiophene. Both chemical shifts and coupling constants are, as expected, in better agreement with those of the selenophene part of selenolo[2,3-*b*]thiophene [17], which exhibits an ABCD pattern. In addition to the proton-proton spin couplings, interactions between the ^{77}Se isotope of spin 1/2 and the protons can be observed. These coupling constants can also be obtained from the uncoupled ^{77}Se NMR spectrum: $^2J_{\text{Se-H}_\alpha} = 48.8$ Hz, $^3J_{\text{Se-H}_\beta} = 9.6$ Hz, $^4J_{\text{Se-H}_\alpha} = 0.8$ Hz, and $^5J_{\text{Se-H}_\beta} = 1.8$ Hz. The decoupled ^{77}Se NMR spectrum shows only one peak at 26.13 ppm, upfield from selenophene used as an external standard. The decoupled ^{13}C NMR spectrum shows, as expected, four peaks: two of high intensity at 124.21 ppm (β -carbons) and 133.84 ppm (α -carbons), and two of low intensity, as expected for quaternary carbons, at 136.15 ppm (C7) and 150.35 ppm (C8), downfield from TMS used as an internal standard. From the uncoupled ^{13}C NMR spectrum the couplings between carbon atoms and ring hydrogens were obtained: $^1J_{\text{C-H}_\alpha} = 187.75$ Hz, $^1J_{\text{C-H}_\beta} = 165.5$ Hz, $^2J_{\text{C-H}_\alpha} = 4.5$ Hz, and $^2J_{\text{C-H}_\beta} = 7.0$ Hz. The assignment of both ^{77}Se and ^{13}C couplings to the hydrogens in the same ring is based on the corresponding couplings in selenophenes [2, 3, 4]. A ^{13}C NMR study of thieno[2,3-*b*]thiophene and some of its 2-substituted derivatives was recently published by Gronowitz et al. [18]. A comparison of the spectra of thieno[2,3-*b*]thiophene and selenolo[2,3-*b*]selenophene reveals that the resonance of all but the C-7 carbon atoms occur at lower fields for the selenolo[2,3-*b*]selenophene.

From the residue after distillation of selenophene, Umezawa [10] claimed the isolation of one liquid and two crystalline selenophenes, besides benzo[*b*]selenophene. By means of combined VPC-mass spectroscopic analyses we could also demonstrate the presence of benzo[*b*]selenophene and the previously described selenolo[3,2-*b*]selenophene, but neither the second crystalline isomer nor the liquid selenophene was found. However, the melting point of authentic selenolo[2,3-*b*]selenophene is 56–57°C, which compares favourably with the value of 51–51.5°C given by Umezawa [10] for the second crystalline selenophene, to which he assigned structure I. In view of our results, we now can conclude that Umezawa's statement that selenolo[2,3-*b*]selenophene (II), is a liquid with b.p. 90–93°C/14 mmHg, is also incorrect.

From the above discussion it is obvious that the structural assignment made by Umezawa [10] should be revised. The high-melting isomer should be assigned structure I, the low-melting, crystalline isomer structure II, and the liquid isomer structure III. This would be in agreement with the corresponding increase in melting point for the three thienothiophenes of the corresponding structures [19, 20].

As mentioned above, we were not able to provide evidence for the presence of any other selenophene than selenolo[3,2-*b*]selenophene(I) among the products of the reaction between acetylene and selenium.

We have, however, carefully investigated the product distribution of this reaction, by carrying out the distillation of the higher-boiling residues after distillation of selenophene. The distillations

were carried out at three different pressures, 760, 12, and 1,5 mmHg, and in such a way that the boiling temperatures of the fractions collected were in intervals of ten degrees. A broader fraction, 123–140°C/12 mmHg, was collected in order to easily isolate the selenolo[3,2-*b*]selenophene formed. This fraction crystallizes either on standing or in the condenser during the distillation, and the pure selenolo[3,2-*b*]selenophene, m.p. 125–127°C, can be obtained after one recrystallization from ethanol. All spectroscopic data for the compound obtained in this way are in accordance with the data reported by Gronowitz et al. [11] for the *trans*-selenophene obtained directly from the residue after distilling off selenophene, and also with the data for an authentic sample prepared in the way described above.

All fractions collected were analysed by means of VPC and some representative fractions by means of combined VPC and mass spectrometry. During optimization of the reaction conditions for preparation of selenophene we ran the reaction at two different temperatures, 350°C and 450°C, and the highest temperature gave the best yields of selenophene. Raising the reaction temperature another 100°C increased the formation of benzene and toluene, which became a serious drawback [7]. The product distribution of the reaction was therefore determined at these

Table I.

No.	Compound	Yield in % $\times 10^{-2}$ based on the selenium used at		Characteri- zation Method				
		350°C	450°C	A	B	C	D	Ref.
1	Selenophene	2 000	5 800	×			×	7
2	Toluene	1.7 ^a	2.1 ^a	×		×	×	(b)
3	Xylene	0.8 ^a	0.06 ^a	×		×	×	(c)
4	2-Methylselenophene	13.2	6.0	×	×		×	23
5	3-Methylselenophene	2.7	3.2	×	×	×		2
6	2-Ethylselenophene	8.1	6.0	×	×		×	24
7	3-Ethylselenophene	6.2	5.1	×	×	×		(d)
8	Diethyldiselenide	27.7	14.5	×	×	×	×	25
9	2- <i>n</i> -Butylselenophene	3.0	1.0	×			×	24
10	2-Methyl-1,3-diselenacyclo- pentene-4	14.6	0.6		×		×	—
11	2-Methylselenoselenophene	7.0	0.4			×	×	26
12	Naphthalene	—	0.13 ^a	×		×	×	(e)
13	2-Ethylselenoselenophene	44.7	2.1	×		×	×	(d)
14	3-Ethylselenoselenophene	6.2	1.2	×		×	×	(d)
15	2-Methylnaphthalene	—	0.05 ^a	×		×	×	(f)
16	1-Methylnaphthalene	—	0.06 ^a	×		×	×	(b)
17	Benzo[<i>b</i>]selenophene	4.4	11.1	×		×	×	27, 28
18	Selenolo[3,2- <i>b</i>]selenophene	54.3	13.9	×		×	×	11 (d)
19	2,2'-Biselenienyl	4.0	7.2	×			×	29 (d)
20	2,3'-Biselenienyl	—	4.5				×	
21	3,3'-Biselenienyl	2.4	3.5	×			×	30 (d)
22	Phenylselenoselenophene	2.3	1.9				×	—
23	Bis(2,2'-selenienyl)selenide	7.0	7.5	×			×	(d)
24	Dibenzoselenophene	2.9	0.3	×			×	31
25	Selenolobenzoselenophenes (3 isomers)	—	3.4				×	—
26	Diselenoloselenophenes (2 isomers)	—	2.0				×	—

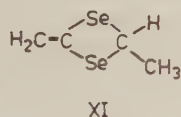
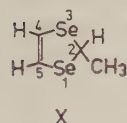
Method of characterization

- Comparison of retention time and mass spectrum with those of authentic sample.
 - Analysis of NMR spectra of the substances obtained by preparative gas chromatography.
 - Comparison of the mass spectrum with published data.
 - Analysis of the fragmentation pattern in the mass spectrum obtained by means of combined gas chromatography and mass spectrometry.
- Based on selenophene formed.
 - Purchased from E. Merck, Darmstadt, Germany.
 - Purchased from Malinkrodt Chemical Works, St. Louis, USA.
 - For preparation, see Experimental Part.
 - Purchased from Kebo AB, Stockholm, Sweden.
 - Purchased from Fluka AG, Buchs, Switzerland.

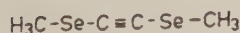
two temperatures. At 450°C, the VPC analysis of the crude reaction product indicated the formation of at least 30 compounds, 4 of which were formed in minor amounts. The structures, total yields, method of characterization, and reference to the preparative procedure or to the published mass spectrum are given in Table I.

The yields, expressed in $\% \times 10^{-2}$, were calculated from the non-calibrated peak area measurements on the gas chromatograph and are based on the selenium used or, for compounds containing no selenium, on the selenophene formed. The compounds in Table I are arranged in order of increasing retention time. Structure assignments of the products formed are derived in all 26 cases from the composition of the molecular ions based on their isotopic clusters and to some extent on the fragmentation patterns (Method D). For 20 compounds, we also confirmed the assignments by comparing their retention times and mass spectra with those of authentic samples, which we synthesized or were in possession of (Method A). In a few cases it was also possible to compare the recorded mass spectra with the published ones (Method C).

It was originally intended to obtain pure compounds by means of preparative gas chromatography (Method B), but as the compounds almost inevitably led to the deterioration of the column, we only used it twice. In the first run, we obtained the two methyl-, the two ethylselenophenes, and the diethyldiselenide, and the second run was aimed at isolation of compound No. 10 in Table I, which could not even tentatively be identified by means of its mass spectrum. The mass spectrum indicated the composition $C_4H_6Se_2$, and the selenium isotope pattern around $m/e = 214$ (M^+) and around $m/e = 199$ ($M^+ - CH_3$) coincided with that simulated for two selenium atoms. Both peaks were of 100% intensity. Single atom selenium patterns were observed at $m/e = 132$ ($M^+ - H_2Se$), $m/e = 105$ (C_2HSe), and $m/e = 93$ ($CHSe$). The presence of a methyl group indicated either some kind of acyclic structure with a triple bond or one of the two cyclic structures X or XI.



Differentiation between the linear and cyclic structures could be obtained through NMR spectral analysis. Preparative gas chromatography yielded enough pure compound to determine its 1H , ^{13}C , and ^{77}Se NMR spectra. The decoupled ^{77}Se NMR spectrum showed only one peak at 130.25 ppm upfield from selenophene used as an external standard, and could therefore be compatible with spectra of both of the cyclic structures X and XI. No symmetrical acyclic diselenide structure with a triple bond and a methyl group could be written, and the only remaining linear structure was compound XII with two isolated selenide groups



XII

The 100 MHz 1H NMR spectrum excluded this structure as it showed the presence of two vinyl protons at 7.12 ppm (s), one proton at 5.19 ppm (q), and three protons at 1.84 ppm (d) downfield from TMS. The coupling between methine and methyl protons was 7.0 Hz. This could still be compatible with both structures X and XI and the final proof was provided by the decoupled ^{13}C NMR spectrum in $CDCl_3$, which showed only

three peaks at 117.76 ppm, 33.19 ppm, and 29.18 ppm downfield from TMS, compatible with compound X. For compound XI, four peaks are expected. From the undecoupled ^{13}C NMR spectrum, the following couplings were obtained $^1J_{C_1-H_1} = 182.34$ Hz, $^2J_{C_1-H_2} = 6.10$ Hz, $^3J_{C_1-H_3} = 3.97$ Hz, $^1J_{C_2-H_4} = 155.09$ Hz, $^3J_{C_2-H_5} = 5.03$ Hz, $^1J_{C_3-H_6} = 129.09$ Hz, and $^2J_{C_3-H_7} = 5.03$ Hz. These coupling constants are in good agreement with the corresponding constants in the structurally related compound 1,4-dithiin [21]. Compound No. 10 was therefore assigned structure X and according to IUPAC rules named 2-methyl-1,3-diselenacyclopentene-4. In a more trivial way, it could also be named 2-methyl-2H-1,3-diselenole. It should be pointed out that the relatively high percentage occurrence of X among the reaction by-products of selenophene preparation only takes place, when the reaction is carried out at 350°C, and drops drastically, when the temperature is increased. In order to examine if the yield of X increases at lower temperatures, we have carried out the reaction between acetylene and selenium at 270°C. As already described by Gronowitz et al. [7], the formation of selenophene is very slow if the reaction temperature is kept below 340°C and it was not surprising that the total yield of the crude reaction product was under 3%. The main reaction products were 2-ethylselenoselenophene (20%) and selenolo[3,2-b]selenophene (40%), which is in accordance with the fact, that yields of both these compounds drop drastically with an increase in temperature (cf. compounds Nos. 13 and 18 in Table I). The interesting compound X was found only in minor amounts, and it seems that a temperature of about 350°C is optimal temperature for its formation.

Inspection of Table I shows that the alkylselenophenes constitute the greatest part of the low molecular compounds formed in the reaction between acetylene and selenium. 2-*n*-Butylselenophene is the highest alkylselenophene found. The 2-substituted alkylselenophenes predominate over the 3-substituted. However, the difference is diminished at the higher temperature. The relatively high yield of 2-methylselenophene, a compound with an odd number of carbon atoms, may be rationalized by the results of Cullis et al. [22], who found that fragments with an odd number of carbon atoms were formed during the pyrolysis of acetylene.

The only acyclic product detected is diethyldiselenide, which is formed in high yields at both temperatures. It is also worth noting the very high yield of 2-ethylselenoselenophene at 350°C and its drastic drop at 450°C, which is also observed for selenolo[3,2-b]selenophene. The opposite, i.e. an increase in yield at higher temperature, characterizes the formation of benzo[b]selenophene. Also the high molecular compounds, such as biselenophenes, selenolobenzoselenophenes, and diselenoloselenophenes are formed in larger amounts at higher temperatures.

Finally, the complexity of the reaction between acetylene and selenium should be stressed, and it should be pointed out that its preparative importance in laboratory scale is primarily limited to the preparation of selenophene and possibly also selenolo[3,2-b]selenophene.

Experimental

The 1H NMR spectra were recorded on a Varian A-60 NMR spectrometer and on a Jeol MH 100 high resolution spectrometer. The ^{13}C NMR spectra were obtained at 15.0 MHz with a Jeol JMN-60 spectrometer with a built-in Jeol 980A computer with 12 K memory. The ^{77}Se NMR spectra were obtained at 19.135 MHz on a Varian XL-100-15 spectrometer equipped with fre-

quency sweep, proton wide band decoupler and Fourier transform operation. Field-frequency control (lock) was effected by means of the deuterium resonance of hexadeuterioacetone. Mass spectra were recorded on an LKB A-9000 mass spectrometer and analytical VPC* was carried out with a Perkin-Elmer 900 gas chromatograph connected to a Varian 480 digital integrator. The integrator was not calibrated. A BDS 10% on Chrom W column was used for all analyses except the compounds with very long retention times (Nos. 22–26 in Table I), where an OV 25 3% on Chrom Q column was used. For the preparative gas chromatography a Perkin-Elmer F21 preparative instrument equipped with a BDS 20% on Chrom W column was used.

Elementary analyses were carried out by Ilse Beetz, Mikroyanalisches Laboratorium, Kronach, Germany.

3-Ethylselenophene. A mixture of 2.6 g (0.015 mol) of 3-acetylselenophene [2], 3.2 g (0.064 mol) of hydrazine hydrate, and 1.2 g (0.048 mol) of sodium hydroxide in 50 ml of ethylene glycol was heated for 0.5 h at 110–120°C, and then for one hour at 170–180°C. Apparatus was then arranged for distillation and all material passing over up to 130°C was distilled off. The resulting distillate was extracted with ether, and the extracts were washed with 2 N hydrochloric acid and water, and dried over magnesium sulphate. The residue after evaporation of the solvent was distilled, yielding 1.7 g (71%) of a colourless liquid, b.p. 54–55°C/14 mmHg, $n_D^{20} = 1.5502$. NMR spectrum (CDCl_3): $\delta_{\text{H}_1} = 7.48$, $\delta_{\text{H}_4} = 7.17$, $\delta_{\text{H}_5} = 7.85$, $\delta_{\text{CH}_3} = 2.55$, $\delta_{\text{CH}_2} = 1.22$, $J_{14} = 1.30$ Hz, $J_{25} = 2.60$ Hz, $J_{45} = 5.20$ Hz, $J_{\text{CH}_3-\text{CH}_2} = 7.40$ Hz.

[Found: C 45.45; H 5.07; Se 49.68; M.wt. 160. Calc. for $\text{C}_6\text{H}_6\text{Se}$: C 45.30; H 5.07; Se 49.63; M.wt. 159.09.]

2-Ethylselenoselenophene. To a solution of 5.3 g (0.04 mol) of selenophene in 50 ml of dry ether, 30 ml of 1.48 N *n*-butyllithium in hexane was added dropwise with stirring under nitrogen at room temperature. The reaction mixture was refluxed for 15 min, then cooled in ice-water, whereupon 9.5 g (0.044 mol) of diethyl diselenide in 50 ml of dry ether was slowly added. When the addition was complete, the reaction mixture was refluxed for one hour, then cooled to 0°C, and 50 ml of 25% solution of ammonium chloride was added. The phases were separated and the water phase extracted twice with ether. The combined ether phases were washed with water, dried over magnesium sulphate and fractionated. After a small fore-run of unreacted diethyl diselenide, 6.3 g (66%) of the title compound, b.p. 102–103°C/10 mmHg, was obtained as a yellow liquid. NMR spectrum (CDCl_3) was analysed as an ABX spectrum: $\delta_{\text{H}_1} = 7.37$, $\delta_{\text{H}_4} = 7.17$, $\delta_{\text{H}_5} = 8.06$, $\delta_{\text{CH}_3} = 2.83$, $\delta_{\text{CH}_2} = 1.43$, $J_{34} = 3.68$ Hz, $J_{35} = 1.19$ Hz, $J_{45} = 5.71$ Hz, $J_{\text{CH}_3-\text{CH}_2} = 7.20$ Hz.

[Found: C 30.29; H 3.37; Se 66.34; M.wt. 240. Calc. for $\text{C}_6\text{H}_6\text{Se}_2$: C 30.27; H 3.39; Se 66.34; M.wt. 238.05.]

3-Ethylselenoselenophene. A solution of 8.4 g (0.04 mol) of 3-bromoselenophene in 70 ml of dry ether was cooled to –70°C, and 30 ml of 1.48 N *n*-butyllithium in hexane was added dropwise with stirring under nitrogen at such a rate that the temperature did not exceed –65°C. After stirring for an additional 15 min at –70°C, a solution of 9.5 g (0.044 mol) of freshly prepared diethyl diselenide in 30 ml of dry ether was added during 15 min. The reaction mixture was allowed to reach room temperature, stirred for 5 hours, then cooled to 0°C, whereupon 50 ml of 25% solution of ammonium chloride was added. The phases were separated and the water phase extracted twice with ether. The combined ether phases were washed with water, dried over magnesium sulphate, and fractionated. After a small fore-run of unreacted diethyl diselenide, 6.0 g (63%) of the title compound, b.p. 126–126.5°C/20 mmHg, was obtained as a light yellow liquid.

NMR spectrum (CDCl_3): an ABX spectrum with a strongly coupled AB part centred at 7.98 ppm, $\delta_{\text{H}_1} = 7.34$, $\delta_{\text{CH}_3} = 2.84$, $\delta_{\text{CH}_2} = 1.41$, $J_{\text{CH}_3-\text{CH}_2} = 7.05$ Hz.

[Found: C 30.44; H 3.38; Se 66.46; M.wt. 240. Calc. for $\text{C}_6\text{H}_6\text{Se}_2$: C 30.27; H 3.39; Se 66.34; M.wt. 238.05.]

2,2'-Biselenienyl. The procedure of Gronowitz and Karlsson [32] for the preparation of 2,2'-bithienyl was followed. To a solution of 13.1 g (0.10 mol) of selenophene in 100 ml of dry ether, 74 ml of 1.48 N *n*-butyllithium in hexane was added dropwise with stirring under nitrogen at room temperature. The reaction mixture was refluxed for 30 min., then cooled in ice-water and 16.1 g (0.12 mol) of anhydrous cupric chloride was added in portions. The reaction mixture was then refluxed for 3 hours, cooled in an ice-bath, and decomposed by careful addition of 100 ml of ice-cold 2 N hydrochloric acid. The cuprous chloride formed was filtered off, the phases were separated, cuprous chloride was washed with 2 N hydrochloric acid, the combined water phases were extracted twice with ether, and the combined ether extracts washed with saturated solution of sodium hydrogen carbonate and water, and dried over magnesium sulphate. Evaporation of the solvent yielded half-crystalline residue, which after recrystallization from petroleum ether gave 6.1 g (47%) of 2,2'-biselenienyl, m.p. 47–48°C; lit. value [29]: m.p. 49°C. NMR spectrum (CDCl_3): an ABX spectrum analyzed and simulated by means of the UEAITR computer program [34]: $\delta_{\text{H}_1} = 7.51$, $\delta_{\text{H}_5} = 7.82$, $\delta_{\text{H}_4} = 7.59$, $J_{23} = 5.40$ Hz, $J_{24} = 3.87$ Hz, $J_{34} = 1.42$ Hz.

3,3'-Biselenienyl. The procedure of Gronowitz and Karlsson [32] for the preparation of 3,3'-bithienyl was followed. A solution of 4.2 g (0.02 mol) of 3-bromoselenophene in 50 ml of dry ether was cooled to –70°C, and 17 ml of 1.30 N *n*-butyllithium in hexane was added dropwise with stirring under nitrogen at such a rate that the temperature did not exceed –65°C. After stirring for an additional 15 min. at –70°C, 3.36 g (0.025 mol) of anhydrous cupric chloride was added in portions. The reaction mixture was allowed to reach room temperature, refluxed for 3 hours, then cooled in an ice-bath, and decomposed carefully with 50 ml of ice-cold 2 N hydrochloric acid. The mixture was worked up as in the synthesis of 2,2'-biselenienyl. Recrystallization from ligroin gave 1.0 g (38.5%) of 3,3'-biselenienyl, m.p. 152–153°C. NMR spectrum (CDCl_3): a strongly coupled ABX spectrum with an AB part centred at 7.98 ppm, and an X part centred at 7.61 ppm.

2-(3-Selenienyl)-1,3-dioxolane. The procedure of Gronowitz et al. [33] for the preparation of 2-(3-thienyl)-1,3-dioxolane was followed. 40 g (0.25 mol) of 3-formylselenophene, 20 g (0.32 mol) of ethylene glycol, 100 ml of dry benzene, and a few crystals of *p*-toluenesulphonic acid were refluxed with a water-separator until no more water separated (17 hours). The benzene layer was then washed with sodium bicarbonate solution and water, dried over magnesium sulphate, and fractionated. After a small fore-run of 3-formylselenophene, 41 g (81%) of the acetal, b.p. 120–122°C/10 mmHg, was obtained. NMR spectrum (CDCl_3): the 24-line pattern of the aromatic protons was analysed as an ABMX spectrum and simulated by means of the UEAITR computer program [34]: $\delta_{\text{H}_1} = 8.05$, $\delta_{\text{H}_4} = 7.38$, $\delta_{\text{H}_5} = 7.94$, $\delta_{\text{CH}} = 5.82$, $\delta_{\text{CH}_2} = 3.95$, $J_{24} = 1.20$ Hz, $J_{25} = 2.56$ Hz, $J_{45} = 5.60$ Hz, $J_{\text{CH},\text{H}_1} = 0.30$ Hz, $J_{\text{CH},\text{H}_4} = 0.70$ Hz, $J_{\text{CH},\text{H}_5} = 0.35$ Hz.

[Found: C 41.49; H 4.07; Se 38.84; M.wt. 204. Calc. for $\text{C}_7\text{H}_8\text{O}_2\text{Se}$: C 41.40; H 3.97; Se 38.88; M.wt. 203.10.]

2-Carboxyselenolo[2,3-*b*]selenophene. The procedure of Bugge [13] for the preparation of 5-carboxyselenolo[2,3-*b*]thiophene was followed. To a solution of 20.3 g (0.01 mol) of 2-(3-selenienyl)-1,3-

dioxolane in 250 ml of dry ether, 137 ml of 0.81 N *n*-butyllithium in ether was added dropwise with stirring under nitrogen at room temperature. The reaction mixture was refluxed for 30 min., then cooled to -30°C , whereupon 8.7 g (0.11 mol) of red amorphous selenium was added in one portion. After stirring for 30 min., the reaction mixture was refluxed for one hour, then cooled to -30°C , before 12.0 g (0.11 mol) of methyl chloroacetate in 50 ml of dry ether was added during 5 min., and the solution stirred for 30 min. After standing overnight at room temperature, the reaction mixture was cooled to 0°C , 100 ml of ice-cold 2 N hydrochloric acid was added, and the mixture was stirred for one hour. The aqueous phase was extracted twice with ether, the combined ethereal solutions were treated with saturated sodium hydrogen carbonate solution and water, then dried over magnesium sulphate. The ether solution was added dropwise to a solution of 7.0 g (0.30 mol) of sodium in 200 ml of absolute ethanol. The ether was distilled off and the residual ethanolic solution refluxed for 5 hours. The alcohol was then distilled off at reduced pressure, the residue was dissolved in water, the resulting solution was extracted with ether and the aqueous phase was acidified with ice-cold 2 N hydrochloric acid leaving 12.5 g (45%) of 2-carboxyselenolo[2,3-*b*]selenophene. Recrystallization from acetic acid gave m.p. $244\text{--}248^{\circ}\text{C}$ with decomposition. NMR spectrum (DMSO- d_6): $\delta_{\text{H}_a} = 8.16$, $\delta_{\text{H}_b} = 7.63$, $\delta_{\text{H}_c} = 8.23$, $J_{45} = 5.60$ Hz. In the mass spectrum, the peaks centred at m/e 280 (M^+ and base peak) showed the same pattern as a spectrum simulated for two selenium atoms.

[Found: C 30.17; H 1.62; Se 56.70; M.wt. 280. Calc. for $\text{C}_7\text{H}_4\text{O}_2\text{Se}_2$: C 30.24; H 1.45; Se 56.80; M.wt. 278.03.]

Selenolo[2,3-*b*]selenophene. 2.78 g (0.01 mol) of 2-carboxyselenolo[2,3-*b*]selenophene was dissolved in 50 ml of freshly distilled quinoline, 1.0 g (0.016 mol) of copper bronze was added and the mixture heated with stirring under nitrogen during 4 hours in a metal-bath at $235\text{--}240^{\circ}\text{C}$. The temperature was then raised to 250°C and 100 ml of quinoline was added at the same rate as a solution of selenolo[2,3-*b*]selenophene in quinoline was distilled off. The residual quinoline in the reaction vessel was distilled under reduced pressure (b.p. $106\text{--}107^{\circ}\text{C}/12$ mmHg), and the combined quinoline phases were cooled with ice, acidified with 2 N hydrochloric acid, and extracted with ether. The ether solution was washed with saturated sodium hydrogen carbonate solution and water, dried over magnesium sulphate and concentrated. The light yellow oil thus obtained was dissolved in *n*-pentane and cooled to 0°C , whereupon colourless crystals precipitated. Recrystallization from *n*-pentane yielded 1.33 g (57%) of selenolo[2,3-*b*]selenophene as colourless, long needles with m.p. $56\text{--}7^{\circ}\text{C}$. Its ^1H , ^{13}C , and ^{77}Se NMR spectra were described in the theoretical part.

In the mass spectrum, the peaks centred at m/e 236 (M^+ and base peak) showed the same pattern as a spectrum simulated for two selenium atoms. Single-atom selenium patterns were observed at m/e 156 ($M^+ - \text{Se}$), m/e 117 (C_3HSe) and m/e 93 (CHSe).

[Found: C 30.90; H 1.86; Se 67.64; M.wt. 236. Calc. for $\text{C}_4\text{H}_4\text{Se}_2$: C 30.80; H 1.72; Se 67.48; M.wt. 234.02.]

2-(3-Bromo-2-selenienyl)-1,3-dioxolane. The procedure of Gronowitz et al. [33] for the preparation of 2-(3-thienyl)-1,3-dioxolane was followed. 22.8 g (0.096 mol) of 3-bromo-2-formylselenophene, 6.0 g (0.11 mol) of ethylene glycol, 100 ml of dry benzene, and a few crystals of *p*-toluenesulphonic acid were refluxed with a water separator until no more water separated (9 hours). The benzene layer was then washed with sodium bicarbonate solution and water, dried over magnesium sulphate and fractionated. After a small fore-run of 3-bromo-2-formyl-

selenophene, 22.2 g (82%) of the acetal, b.p. $125\text{--}127^{\circ}\text{C}/0.7$ mmHg, was obtained. NMR spectrum (acetone- d_6): $\delta_{\text{H}_a} = 7.25$, $\delta_{\text{H}_b} = 8.16$, $\delta_{\text{CH}} = 6.00$, $\delta_{\text{CH}_2} = 4.05$, $J_{45} = 5.80$ Hz, $J_{\text{CH}-\text{H}_a} = 0.60$ Hz.

[Found: C 29.95; H 2.56; M.wt. 282/284. Calc. for $\text{C}_7\text{H}_7\text{BrO}_2\text{Se}$: C 29.81; H 2.50; M.wt. 282.00.]

2-Carboxyselenolo[3,2-*b*]selenophene. A solution of 19.4 g (0.067 mol) of 2-(3-bromo-2-selenienyl)-1,3-dioxolane in 75 ml of dry ether was cooled to -70°C and 90 ml of 0.81 N *n*-butyllithium in ether was added dropwise with stirring under nitrogen at such a rate that the temperature did not exceed -65°C . After stirring for an additional 30 min at -70°C , 5.7 g (0.073 mol) of red amorphous selenium was added in one portion and the reaction mixture was allowed to reach room temperature, refluxed for 15 min, then cooled to -30°C , before 7.9 g (0.073 mol) of methyl chloroacetate in 50 ml of dry ether was added dropwise. The mixture was stirred for one hour and left overnight, then cooled to 0°C and hydrolysed with 70 ml of ice-cold 2 N hydrochloric acid. After stirring for one hour, the aqueous phase was extracted twice with ether, the combined ethereal solutions washed with sodium bicarbonate solution and water, then dried over magnesium sulphate. The ether solution was added dropwise to a solution of 4.8 g (0.21 mol) of sodium in 100 ml of absolute ethanol, the ether was distilled off and the residual ethanolic solution was refluxed for 5 hours. The ethanol was then distilled off at reduced pressure, the residue was dissolved in water, the resulting solution was extracted with ether and the aqueous phase was acidified with ice-cold 2 N hydrochloric acid, leaving 10.1 g (36%) of 2-carboxyselenolo[3,2-*b*]selenophene. Recrystallization from ethanol/water (50:50) gave m.p. $217.5\text{--}219^{\circ}\text{C}$. The NMR and mass spectra are in accordance with those obtained for 2-carboxyselenolo[3,2-*b*]selenophene prepared by metallation and carbonation of selenolo[3,2-*b*]selenophene (see below).

2-Carboxyselenolo[3,2-*b*]selenophene. To a solution of 7.0 g (0.03 mol) of selenolo[3,2-*b*]selenophene, obtained from the reaction between acetylene and selenium, in 250 ml of dry ether, 27 ml of 1.23 N *n*-butyllithium in hexane was added dropwise with stirring under nitrogen at room temperature. The reaction mixture was refluxed for 30 min and then poured onto crushed carbon dioxide covered with dry ether. After the temperature has risen to 0°C , 15 ml of water was added, the phases were separated, and the organic phase extracted twice with 2 N sodium hydroxide solution. The combined water phases were washed with ether and carefully acidified with ice-cold 2 N hydrochloric acid, leaving 7.5 g (89.9%) of 2-carboxyselenolo[3,2-*b*]selenophene. Recrystallization from ethanol/water (50:50) gave m.p. $217.5\text{--}219^{\circ}\text{C}$. NMR spectrum (acetone- d_6): $\delta_{\text{H}_a} = 8.34$, $\delta_{\text{H}_b} = 8.44$, $\delta_{\text{H}_c} = 7.75$, $\delta_{\text{CO}_2\text{H}} = 8.84$, and $J_{45} = 5.75$ Hz. In the mass spectrum the peaks centred at m/e 280 (M^+ and base peak) showed the same pattern as a spectrum simulated for two selenium atoms.

[Found: C 31.27; H 1.67; Se 56.74; M.wt. 280. Calc. for $\text{C}_7\text{H}_4\text{O}_2\text{Se}_2$: C 30.24; H 1.45; Se 56.80; M.wt. 278.03.]

Selenolo[3,2-*b*]selenophene. To a solution of 7.0 g (0.025 mol) of 2-carboxyselenolo[3,2-*b*]selenophene in 100 ml of freshly distilled quinoline, 2.5 g (0.039 mol) of copper bronze was added and the mixture heated to 180°C with stirring in a nitrogen atmosphere during 2 hours. Thereafter the reaction mixture was refluxed for 4 hours, the quinoline and liquid selenophene were distilled off and the distillate was acidified with ice-cold 2 N hydrochloric acid and extracted with ether. The ether extract was washed with saturated sodium hydrogen carbonate solution and water, dried over magnesium sulphate and concentrated.

The half-crystalline residue thus obtained was recrystallized from ethanol to yield 3.6 g (61.5%) of selenolo[3,2-b]selenophene as light yellow crystals with m.p. 125–127°C. All spectroscopic data were in accordance with those for the selenolo[3,2-b]selenophene formed in the reaction between acetylene and selenium and isolated as described by Gronowitz et al. [11].

Bis(2,2'-selenienyl)selenide. To a solution of 1.36 g (0.015 mol) of selenophene in 20 ml of dry ether, 11.5 ml of 1.43 N *n*-butyllithium in hexane was added dropwise with stirring under nitrogen at room temperature. The reaction mixture was refluxed for 15 min, then cooled in ice-water, whereupon 1.30 g (0.0165 mol) of red amorphous selenium was added in one portion. After stirring for 30 min, the reaction mixture was refluxed for one hour, then cooled in ice-water, before a solution of 2.80 g (0.013 mol) of 2-bromoselenophene in 20 ml of dry ether was added during 5 min. and the solution stirred for 30 min. After standing overnight at room temperature, the reaction mixture was cooled to 0°C, 15 ml of ice-cold 2 N hydrochloric acid was added, and the mixture was stirred for one hour. The aqueous phase was extracted twice with ether, the combined ethereal solutions were treated with water and saturated sodium hydrogen carbonate solution, then dried over magnesium sulphate. The ether was then distilled off at reduced pressure to give 3.9 g (88%) of a yellow oil, the mass spectrum of which indicated the presence of both selenide (*m/e* 342) and diselenide (*m/e* 422). In order to purify the selenide, the oil was fractionated and 2.1 g (48%) of the product, b.p. 133–134°C/0.005 mmHg, was collected.

In the mass spectrum, no peaks due to the diselenide could be detected, and the peaks due to the molecular ion centred at *m/e* 342 showed the same pattern as the spectrum simulated for three selenium atoms.

[Found: C 28.22; H 1.87; Se 69.91; M.wt. 342. Calc. for $C_4H_4Se_3$: C 28.34; H 1.78; Se 69.27; M.wt. 339.02.]

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References

- Gronowitz, S. and Frejd, T., *Acta Chem. Scand.* 1976, B30, 439.
- Gronowitz, S., Johnson, I. and Hörnfeldt, A.-B., *Chemica Scripta* 1975, 7, 111.
- Fringuelli, F., Gronowitz, S., Hörnfeldt, A.-B., Johnson, I. and Taticchi, A., *Acta Chem. Scand.* 1974, B28, 175.
- Gronowitz, S., Johnson, I. and Hörnfeldt, A.-B., *Chemica Scripta* 1975, 8, 8.
- Gronowitz, S., Westerlund, C. and Hörnfeldt, A.-B., *Acta Chem. Scand.* 1976, B30, 391.
- Cederlund, B. and Hörnfeldt, A.-B., *Acta Chem. Scand.* 1976, B30, 101.
- Gronowitz, S., Frejd, T., Moberg-Ogard, A. and Trege, L., *J. Heterocycl. Chem.*, in press.
- Mazza, F. P. and Solazzo, L., *Rend. Accad. Sci. fis. mat. (Napoli)* 1927, 33, 236. *C. A.* 1929, 23, 2417.
- Briscoe, H. V. A., Peel, J. B. and Robinson, P. L., *J. Chem. Soc.* 1928, 2628.
- Umezawa, S., *Bull. Soc. Chem. Japan* 1939, 14, 363.
- Gronowitz, S., Frejd, T. and Hörnfeldt, A.-B., *Chemica Scripta* 1974, 5, 236.
- Gronowitz, S. and Persson, B., *Acta Chem. Scand.* 1967, 21, 812.
- Bugge, A., *Acta Chem. Scand.* 1969, 23, 1823.
- Kvitko, I. Ya., Sokolova, N. B. and Efros, L. S., *Khim. Geterots. Soedin.* 1973, 715.
- Bugge, A., Gestblom, B. and Hartmann, O., *Acta Chem. Scand.* 1970, 24, 105.
- Read, J. M., Mathis, C. T. and Goldstein, J. H., *Spectrochim. Acta* 1965, 21, 85.
- Bugge, A., Gestblom, B. and Hartmann, O., *Acta Chem. Scand.* 1970, 24, 1953.
- Gronowitz, S., Johnson, I. and Bugge, A., *Acta Chem. Scand.* 1976, B30, 417.
- Challenger, F. and Harrison, J. B., *J. Inst. Pet.* 1935, 21, 135.
- Wynberg, H. and Zwanenburg, O. J., *Tetrahedron Lett.* 1967, 761.
- Butler, R. S., Kead, J. M., Jr and Goldstein, J. H., *J. Mol. Spectrosc.* 1970, 35, 83.
- Cullis, S. F. and Franklin, N. H., *Proc. Roy. Soc. A* 1964, 280, 139.
- Yurev, Yu. K., Mezentsova, N. N. and Vaskovsky, V. E., *Zh. Obshch. Khim.* 1957, 27, 3155.
- Yurev, Yu. K. and Sadovaya, N. K., *Zh. Obshch. Khim.* 1961, 31, 3535.
- Bogolyubov, G. M., Grishin, N. N. and Petrov, A. A., *Zh. Obshch. Khim.* 1969, 39, 2244.
- Chizhov, O. S., Zolotarev, B. M., Sukiasian, A. N., Litvinov, V. P. and Goldfarb, Ya. L., *Org. Mass Spectrom.* 1970, 3, 1379.
- Buu-Hoi, N. P., Mangane, M., Renson, M. and Christiaens, L., *J. Chem. Soc. B* 1969, 971.
- Renson, M., *Chemica Scripta* 1975, 8A, 29.
- Chierici, L., Dell'Erba, C., Guareschi, A. and Spinelli, D., *Ric. Sci. A* 1965, 8, 1537.
- Dell'Erba, C., *Corsi Semin. Chim.* 1968, 175.
- McCullough, J. D., Campbell, T. W. and Gould, E. S., *J. Am. Chem. Soc.* 1950, 72, 5753.
- Gronowitz, S. and Karlsson, H.-O., *Arkiv Kemi* 1960, 17, 89.
- Gronowitz, S., Gestblom, B. and Mathiasson, B., *Arkiv Kemi* 1962, 20, 407.
- Johannesen, R. B., Ferretti, J. A. and Harris, R. K., *J. Magn. Res.* 1970, 3, 84.

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Paper B

Electrophilic Substitution in Selenolo [3,2-b] selenophene
and Selenolo [3,2-b] thiophene - A Quantitative Study.

Electrophilic Substitution in Selenolo[3,2-*b*]selenophene and Selenolo[3,2-*b*]thiophene — A Quantitative Study

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Abstract

*Electrophilic substitution in selenolo[3,2-*b*]selenophene and selenolo[3,2-*b*]thiophene — a quantitative study.* Gronowitz, S.; Konar, A.; Litvinov, V. (Division of Organic Chemistry 1, Chemical Center, University of Lund, P.O. Box 740, S-220 07 Lund, Sweden and Zelinsky Institute of Organic Chemistry, USSR Academy of Sciences, Leninsky Prospekt 47, Moscow, USSR).

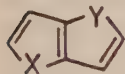
The reactivity of selenolo[3,2-*b*]selenophene and selenolo[3,2-*b*]thiophene, relative to thieno[3,2-*b*]thiophene, towards electrophilic reagents, has been studied by means of competitive experiments. The overall reactivity order was found to be: selenolo[3,2-*b*]selenophene > selenolo[3,2-*b*]thiophene > thieno[3,2-*b*]thiophene, in agreement with existing data that demonstrate a higher rate of electrophilic substitution in selenophene than in thiophene. The three electrophilic substitution reactions studied, namely acetylation, formylation and chlorination, gave rise only to the α -substituted derivatives, and thus no partial relative reactivities of the β -positions could be calculated. From the literature, the overall relative reactivities of the title compounds could also be determined relative to thiophene, and in the case of acetylation and formylation, relative to selenophene.

Introduction

Many quantitative studies on electrophilic substitution and related reactions of five-membered heteroaromatic systems have been carried out in the last two decades, and were reviewed in 1971 by Marino [1]. The relative reactivities of pyrrole, furan, thiophene and selenophene, and subsequently of tellurophene as well [2], towards electrophilic substitution have been determined by the use of kinetic or competitive procedures.

The effect of benzo[*b*]fusion has also been extensively studied (cf. Ref. 1), and here too results concerning the reactivity of benzo[*b*]tellurophene have recently been included [3].

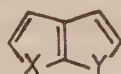
There are, however, comparatively few quantitative data available in the literature concerning the reactivity of compounds formed by the fusion of two five-membered heterocyclic rings, such as thienothiophenes I and IV, selenolothiophenes II and V, or selenoloselenophenes III and VI.



I X = S; Y = S

II X = S; Y = Se

III X = Se; Y = Se



IV X = S; Y = S

V X = S; Y = Se

VI X = Se; Y = Se

Electrophilic attack on thienothiophenes I and IV results in 2-substituted compounds, the second electrophilic substituent entering the other free α -position, i.e. position 5. (For a review, cf. Ref. 4 and references therein.) Although lithiation by hydrogen abstraction by *n*-butyllithium proceeds by a different mechanism, it again results in 2-substitution of I and IV.

Until a few years ago, there was no quantitative comparison of overall reactivities in electrophilic substitution of thieno-

thiophenes. In 1970, Goldfarb *et al.* [5] published a paper on the kinetics of dedeuteriation of mono- and dideutero derivatives of the thienothiophenes I and IV, as well as of benzo[*b*]thiophene, and in 1972, Bugge [6] presented a quantitative study of the acetylation, formylation and chlorination of the two thienothiophenes I and IV.

In both papers, thienothiophenes I and IV were shown to be more reactive than thiophene; in deuterio exchange and acetylation, the reactivities of I and IV were similar, while in formylation and chlorination I was somewhat more reactive than IV.

The rates of base-catalyzed deuterium exchange of thiophene and thienothiophenes I and IV have also been determined by Goldfarb *et al.* [7], and Bugge [8] had shown by competitive metalation experiments with *n*-butyllithium, that I and IV were approximately 6 times more reactive than thiophene.

To the best of our knowledge, there are only two reports concerning electrophilic substitution reactions of the selenium analogues of thienothiophenes. In 1939, Umezawa [9] obtained a tetrabromo and a 2-nitro derivative of selenolo[3,2-*b*]selenophene (III), and a tetrabromo derivative of VI, but he assigned erroneous structures to them and in 1976 Goldfarb *et al.* [10] studied the bromination and formylation of selenolo[3,2-*b*]thiophene (II) and its [2,3-*b*]-annelated isomer (V). Vilsmeier formylation of II gave a mixture of its 2- and 5-formyl derivatives in a ratio of 35:65, and in the case of V, a similar mixture was formed in a ratio of 45:55. Bromination of V with one equivalent of NBS resulted in a mixture containing 20 % of the 2,5-dibromo derivative and 65 % of both 2- and 5-monobromo derivatives in a ratio of 13:87. Similarly, bromination of II gave 20 % of the 2,5-dibromo derivative, but only one monobrominated product in 70 % yield, which was shown to be 5-bromoselenolo[3,2-*b*]thiophene. Its preferential formation was assumed to be due to the primary attack of bromine on the selenium ring atom.

To date, there has been no quantitative comparison of overall reactivities in electrophilic substitution of selenolo-selenophenes and -thiophenes, and this paper is meant to fill this gap.

Results

Overall relative reactivities

Isotope exchange is a technique which relatively quickly and easily gives reliable comparative data on both the electrophilic and protophilic reactivity of the parent five-membered heterocycles, revealing how the activity of their hydrogen atoms varies with position on the ring. This technique was also applied for studying electrophilic [5] and protophilic [7] substitution of the two thienothiophenes I and IV. We have tried to carry out such studies with compounds II and III, but failed owing to the lability of both systems under the conditions required. We have instead studied tin(IV) chloride-catalyzed acetylation

with acetic anhydride in 1,2-dichloroethane, Vilsmeier formylation, and chlorination with *N*-chlorosuccinimide in glacial acetic acid of II and III, *i.e.* the same three reactions examined by Bugge [6] for the thienothiophenes I and IV. We have also tried to maintain exactly the same experimental conditions as Bugge, and we did so for the following reasons. It is known from the work of Bugge [6] that thieno[3,2-*b*]thiophene (I) is 3 times more reactive than thiophene in acetylation, 33 times more reactive in chlorination, and 44 times in formylation. We expected selenolo[3,2-*b*]thiophene (II) and selenolo[3,2-*b*]selenophene (III) to be even more reactive than I, which would create experimental difficulties in the detection of acetyl-, chloro- and formylthiophene, *i.e.* products of the competitive experiments which would be formed in comparatively very small amounts if the reactions were run relative to thiophene. Indeed, some preliminary experiments showed that only competitive acetylations of II and III relative to thiophene could be evaluated, as 2-chloro-, and 2-formylthiophene were formed in amounts not allowing their quantitative determination. As the overall reactivities of thieno[3,2-*b*]thiophene (I) relative to thiophene are known [6], we have decided to run all the competitive experiments relative to I and maintain the same experimental conditions as Bugge. This would enable us to extrapolate the results relative to thiophene, and in the case of acetylation and formylation also to selenophene, as the relative reactivities of selenophene and thiophene are known for these two reactions [2].

The competitive experiments were carried out at three different concentrations to establish whether or not any concentration effects were operative. However, the calculated overall relative reactivities were within the experimental error. All parallel reaction mixtures were made up from the same stock solutions of the reagents and were reacted simultaneously at 25°C in the same thermostated water-bath. The reaction times were 2 days for acetylations, 4 days for formylations and 10 h for chlorinations. The quantitative compositions of the mixtures were established by gas chromatography using the internal standardization method. The molar percentages of all components in the reaction mixtures were evaluated from the peak areas after making the necessary corrections for detector sensitivity for the different compounds. For this reason we have synthesized the 2-acetyl, 2-chloro and 2-formyl derivatives of selenolo[3,2-*b*]selenophene (III), and 5-acetyl-selenolo[3,2-*b*]thiophene. In other cases, we assumed that the detector sensitivity for the derivatives of II substituted in the selenophene and thiophene moiety, respectively, was approximately the same and equal to the sensitivity for the 2-substituted derivative of III. The calculated overall reactivity ratios are collected in Table I, together with the extrapolated values relative to thiophene, and in the case of acetylation and formylation, also relative to selenophene. Extrapolations relative to thiophene were done according to the formula:

$$\frac{K_{XY}}{K_S} = \frac{K_{XY}}{K_{SS}} \cdot \frac{K_{SS}}{K_S}$$

where values of K_{SS}/K_S were taken from Bugge [6] as 2.97, 44.4 and 33.2 for acetylation, formylation and chlorination, respectively. Similarly, in extrapolating the reactivities of II and III relative to selenophene, we used the formula:

$$\frac{K_{XY}}{K_{Se}} = \frac{K_{XY}}{K_S} \cdot \frac{K_S}{K_{Se}}$$

with K_{Se}/K_S values reported by Marino *et al.* [2]. For acetylation, the K_{Se}/K_S value was calculated to be 2.28 by means of the competitive experiments, and for formylation this ratio was determined by means of the measurements of the rate constants of thiophene and selenophene at five different temperatures. The ratio at 25°C was 5.17, and this value was used

Table I. The reactivities of II and III relative to I, thiophene and selenophene

	Acetylation	Formylation	Chlorination
K_{SSc}/K_{SS}	1.69	4.59	4.19
K_{Sese}/K_{SS}	2.81	14.3	10.5
K_{Sese}/K_{SSc}	1.66	3.12	2.50
K_{Sse}/K_S	5.02	204	139
K_{Sese}/K_S	8.35	635	347
K_{Ssc}/K_{Se}	2.20	39.4	—
K_{Sese}/K_{Se}	3.66	123	—

Abbreviations:

SS	thieno[3,2- <i>b</i>]thiophene
SSe	selenolo[3,2- <i>b</i>]thiophene
SeSe	selenolo[3,2- <i>b</i>]selenophene
S	thiophene
Se	selenophene

in our calculations, as all reactions studied by us were carried out at this temperature.

The overall reactivity ratios were calculated from the equation [11]:

$K_{XY}/K_{SS} = (\log[XY]_i - \log[XY]_f) / (\log[SS]_i - \log[SS]_f)$ where XY denotes II or III, SS-thieno[3,2-*b*]thiophene (I) and $[]_i$ and $[]_f$ —initial and final concentrations, respectively.

The ratios for selenolo[3,2-*b*]thiophene (II) were calculated from the sum of the concentrations of its 2- and 5-substituted derivatives, except for chlorination, where only one isomer was formed.

Partial relative reactivities

With knowledge of the overall reactivities of II and III relative to I or thiophene and the isomer distributions in the reactions, it is possible to calculate the reactivities of the different positions in II and III. However, the three electrophilic substitution reactions studied gave rise only to the α -substituted derivatives, and thus only the partial relative reactivities of the two α -positions of the unsymmetrical selenolo[3,2-*b*]thiophene (II) could be determined. As already mentioned, the Vilsmeier formylation of II was studied by Goldfarb *et al.* [10], who determined the ratio of the 2- and 5-substituted formyl derivatives to 35:65. In the present study, we found this ratio to be 27:73, and the corresponding ratio in acetylation 44:56. However, we could only find one substitution product in the NCS-chlorination of II, which might have been expected in view of the results of the NBS-bromination of II, where besides the 2,5-dibromo derivative, only one monobrominated product was formed [10]. By means of its ^1H NMR spectrum, where the coupling between hydrogens of the thiophene ring was observed, it was shown to be a product of bromination at the 5-position, *i.e.* in the selenophene part of the molecule, and analogously, we could also expect 5-substitution in the case of NCS-chlorination of II. In order to confirm this, we have carried out a reaction of II with one equivalent of NCS, and indeed found that only one monosubstituted product was formed. No dichloro derivative could be detected. However, the structural assignment could not be based on the ^1H NMR spectrum as it was of the strongly coupled ABC-type, and no apparent coupling constants could be directly observed. This spectrum was analyzed and simulated by means of the UEAIR computer program [12] and is given in the Experimental Part. The assignment of the monochloro derivative was instead based on its ^{13}C NMR spectrum and comparison with the spectrum of II, and the known substituent effects in the ^{13}C NMR spectra of 2-substituted thieno[3,2-*b*]thiophenes [13], and 2-substituted selenolo[3,2-*b*]selenophenes [14]. This confirmed the proposed structure

Table II. Isomer distribution and partial reactivities of the 2- and 5-positions of II relative to α -positions in I, thiophene or selenophene

	Acetylation	Formylation
$K_{\text{SSe-2}}/K_{\text{SS-2}}$	1.46	2.41
$K_{\text{SSe-5}}/K_{\text{SS-2}}$	1.89	6.70
$K_{\text{SSe-5}}/K_{\text{SSe-2}}$	1.29	2.78
$K_{\text{SSe-2}}/K_{\text{S}}$	4.34	107
$K_{\text{SSe-5}}/K_{\text{Se}}$	2.46	57.5
% 2-SSeX: % 5-SSeX	44:56	27:73

of 5-chloroselenolo[3,2-*b*]thiophene. Isomer distribution and the calculated partial relative reactivities of the 2- and 5-positions of II, together with the extrapolated values relative to thiophene and selenophene, are collected in Table II. The reactivity of the 2-position was compared with the α -position of thiophene, and the reactivity of the 5-position with the α -position of selenophene. The required values of the reactivity ratios of selenophene relative to thiophene were the same as in Table I (cf. Ref. 2).

Discussion

As can be seen from Table I, the overall relative reactivities vary with the nature of electrophile, but the following order of reactivity is always maintained:



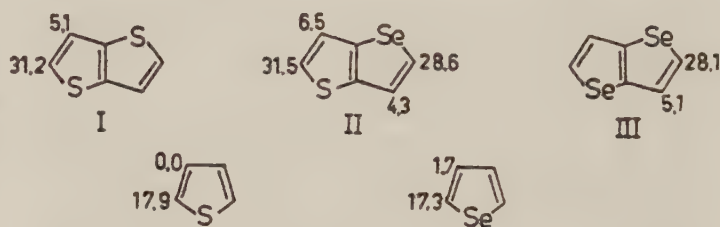
With an electrophilic reagent such as the tin(IV) chloride-acetic anhydride adduct, the "selectivity" is poor: III is only 1.7 times more reactive than II, 2.8 times more reactive than I, and 8.3 times more reactive than thiophene. In NCS chlorination and Vilsmeier formylation, the difference in reactivity between III and II is increased to 2.5 and 3.1 times, respectively, but the reactivity ratios between III and thiophene are increased drastically to 347 and 635. For both II and III the overall reactivity ratios relative to I increase in the series: acetylation < chlorination < formylation, which is in agreement with the results of Bugge [6] for the ratios of I and IV relative to thiophene. The overall order of reactivities in all three reactions is, as already mentioned, $\text{III} > \text{II} > \text{I}$. This order could be expected on the basis of the existing experimental data, which show higher rates of electrophilic substitution in selenophene than in thiophene (Ref. 1, p. 279), under the assumption that these results can also be extrapolated to include condensed systems like I–III.

A brief inspection of Table II reveals that the electrophilic substitution of II occurs more readily in its selenophene than thiophene moiety by a factor of 1.3 for acetylation and 2.8 for formylation. This is also reflected in the isomer distribution between 2- and 5-substituted derivatives. Both positions are also more reactive than their counterparts in non-condensed systems, i.e. thiophene and selenophene, respectively. The reactivity of the 2-position seems to be more enhanced relative to thiophene than that of the 5-position relative to selenophene.

We have also tried to rationalize the results obtained on the basis of existing quantum mechanical calculations. In the literature there is quite a number of publications dealing with calculations of reactivities and theoretical electronic spectra of the isomeric thienothiophenes and dithienothiophenes. (For a review, see Ref. [4] and references therein.). At first, these calculations were developed mainly in the π -electron

approximation, but recently, semiempirical methods including all valence electrons have also been used with good results. However, there are comparatively few data concerning quantum chemical calculations on the selenium analogues of thienothiophenes. Gleiter *et al.* [15] used a parametrized HMO procedure and the semiempirical PPP-, and EWMO-methods to assign the photoelectron spectra of I, II, III and their [2,3-*b*]-annulated isomers. In order to estimate the reactivities for electrophilic substitution at various positions of the isomeric thienothiophenes, selenolothiophenes and selenoloselenophenes, Goldfarb *et al.* [16] performed a quantum chemical analysis of thiophene, selenophene and the above-mentioned systems by using a semi-empirical LCAO SCF MO method including all valence electrons.

To estimate reactivity, many indices have been proposed, of which the localization energy is the most adequate and convenient. This measure was also used by Goldfarb *et al.* [16], who estimated the reactivities from the difference between the bond energies of the initial molecule and its protonated form (σ -complex), i.e. the energy of localization ΔA^+ . The values of ΔA^+ for I–VI, as well as for thiophene and selenophene, in relation to the 3-position of thiophene, were estimated, and those relevant to the present work are shown below.



A brief inspection of these results shows that these are in agreement with experimental data, only in regard to the predominant 2-substitution in I, II and III, and in regard to their higher overall reactivity compared to that of thiophene or selenophene.

However, the values obtained give an incorrect picture of the systems' mutual reactivity order as well as of the reactivity ratio of positions 2 and 5 in selenolo[3,2-*b*]thiophene (II). This is not surprising, if one notes that the incorrect reactivity order is also obtained for the parent compounds thiophene and selenophene.

Experimental

The gas chromatographic analyses were carried out with a Perkin-Elmer 900 gas chromatograph equipped with a flame ionization detector and connected to a Varian 480 integrator. The integrated peak areas were corrected for varying detector sensitivity. The corrections were made for unsubstituted I, II and III, for the 2-acetyl, 2-chloro and 2-formyl derivatives of I and III, and for 5-acetylselenolo[3,2-*b*]thiophene. The sensitivity for the 2-acetyl derivative of II was assumed to be equal to that for the 5-acetyl derivative, and the sensitivities for the 2- and 5-chloro and 2- and 5-formyl derivatives of II were assumed to be equal to each other and to those for the 2-chloro and 2-formyl derivatives of I. A Dexil 300 3 % on Chromosorb W AW column was used for all analyses, and all compounds discussed above were identified by comparison of their retention times with that of the corresponding authentic sample. In the case of the derivatives of II, the identification was made by means of their mass spectra, obtained on an LKB A-9000 mass spectrometer coupled with a gas chromatograph. NMR spectra were recorded on a JEOL MH 100 high resolution spectrometer. Elementary analyses were carried out by Ilse Beetz, Mikroanalytisches Laboratorium, Kronach, Germany.

2-Acetylselenolo[3,2-*b*]selenophene. To a cooled solution of 1.17 g (0.0050 mol) of selenolo[3,2-*b*]selenophene in 15 ml of 1,2-dichloroethane, a mixture of 0.56 g (0.0055 mol) of acetic anhydride and 1.43 g (0.0055 mol) of tin(IV)chloride was added dropwise with stirring under nitrogen at 0°C. A red colour of the solution appeared during the addition of the acetylating agent. The reaction mixture was stirred overnight at room temperature and hydrolysed with 2 N sodium hydroxide solution. The organic layer was washed with 2 N sodium hydroxide solution and water, and dried over magnesium sulfate. Evaporation of the solvent left 1.0 g (72.4 %) of the crude reaction product, which after two recrystallizations from petroleum ether (65–70°C) gave 820 mg (59.4 %) of the title compound, as yellow prisms, m.p. 114–115°C. NMR (acetone-*d*₆); δ (ppm): 8.39 (d, 1H, H₃), 8.40 (d, 1H, H₅), 7.70 (2×d, 1H, H₄), 2.56 (s, 3H, CH₃); $J_{H_5-H_6}$ =6.0 Hz, $J_{H_3-H_6}$ =0.8 Hz. Anal. Calcd. for C₈H₄OSe₂: C 34.81; H 2.19; Se 57.20. Found: C 35.19; H 2.24; Se 56.71. In view of this NMR spectrum, we found Bugge's assignments for 2-acetylthieno[3,2-*b*]thiophene [6]: δ (ppm): 7.90-H₄ and 7.50-H₅, curious. As we had access to the compound, we reevaluated its NMR spectrum to be: NMR (acetone-*d*₆); δ (ppm): 8.13 (d, 1H, H₃), 7.84 (d, 1H, H₅), 7.44 (2×d, 1H, H₄), 2.58 (s, 3H, CH₃); $J_{H_5-H_6}$ =5.5 Hz, $J_{H_3-H_6}$ =0.6 Hz.

2-Chloroselenolo[3,2-*b*]selenophene and 2-selenolo[3,2-*b*]selenophene aldehyde. The preparations of these two compounds will be described in another publication [14].

5-Acetylselenolo[3,2-*b*]thiophene. This compound was prepared from the corresponding acid [17] and methyllithium according to the general procedure described in Ref. 18.

To a cooled solution (0°C) of 2.31 g (0.010 mol) of 5-carboxy-selenolo[3,2-*b*]thiophene, 75 ml of a 0.33 N ethereal solution of methyllithium was added dropwise with stirring under a nitrogen atmosphere. During the addition, which took 30 min, a yellow precipitate separated and then redissolved as the addition was continued. The resulting solution was refluxed for 2 hours, and then poured into ice-cold 2 N hydrochloric acid. The organic phase was separated, the water phase was washed twice with ether, the combined ethereal extracts were washed with aqueous sodium carbonate solution, dried over magnesium sulphate and concentrated. The resulting half-crystalline residue was recrystallized from cyclohexane, giving 1.56 g (68 %) of light yellow crystals, m.p. 102–104°C. NMR (CDCl₃); δ (ppm): 7.75 (d, 1H, H₃), 7.54 (2×d, 1H, H₅), 8.30 (d, 1H, H₄), 2.57 (s, 3H, CH₃); $J_{H_2-H_3}$ =5.6 Hz, $J_{H_3-H_6}$ =0.7 Hz. Anal. Calcd. for C₈H₄OSe: C 41.93; H 2.64; S 13.99; Se 34.46. Found: C 42.12; H 2.57; S 14.11; Se 35.27.

Chlorination of selenolo[3,2-*b*]thiophene with one equivalent of *N*-chlorosuccinimide (NCS). A solution of 531 mg (3.0 mmol) of selenolo[3,2-*b*]thiophene in 50 ml of glacial acetic acid was thermostated to 25±0.1°C. To the solution, 400 mg (3.0 mmol) of NCS was added all at once, and the reaction mixture was stirred for 24 h in the dark. It was then poured into water, extracted with ether, and the combined ether extracts were washed with 2 N sodium hydroxide solution and water, dried over magnesium sulfate and concentrated. The resulting oily residue was analyzed by means of GLC and shown to consist of 13 % of the unreacted selenolo[3,2-*b*]thiophene, and only one more product with the same retention time as that of the chlorination product of II in the competitive experiments. The mass spectrum confirmed the structure of a mono-chlorinated compound. The peaks centred at *m/e* 222 (M⁺ and base peak) exhibited the same pattern as a spectrum simulated for one selenium, one sulfur and one chlorine atom. The oil was then dissolved in *n*-pentane, decolourized with active carbon and the pentane solution cooled to 0°C leaving 286 mg (43 %) of light yellow crystals, m.p. 49–52°C. The structure of the 5-chloroselenolo[3,2-*b*]thiophene was confirmed by its ¹³C NMR spectrum, which showed a downfield shift compared

to II and a low intensity of the substituent 5-carbon. The ¹H NMR spectrum was strongly coupled, and was evaluated by means of the UEAIR computer program [12] to give the following chemical shifts and coupling constants: NMR (acetone-*d*₆); δ (ppm): 7.55 (H₂), 7.38 (H₃), 7.49 (H₄); $J_{H_2-H_3}$ =5.4 Hz, $J_{H_3-H_6}$ =0.7 Hz.

¹³C NMR (acetone-*d*₆); δ (ppm) downfield from TMS used as an internal standard: 127.3 (C₁), 123.0 (C₂), 134.9 (C₅). 123.5 (C₆), 138.8 (C₇), 140.6 (C₈).

Table III. *Competitive acetylations*

Initial conc. of reactants in mmoles			Final conc. of products in mmoles		Reactivity relative to I
Ac ₂ O	SSe	SS	SSeAc	SSAc	K _{XY} /K _{SS}
64.00	66.67	66.67	7.75	4.75	1.67
48.00	50.00	100.00	4.09	4.92	1.69
38.40	40.00	120.00	2.75	4.87	1.72
Average					1.69
	SeSe		SeSeAc		
64.00	66.67	66.67	9.45	3.54	2.80
48.00	50.00	100.00	5.18	3.77	2.85
38.40	40.00	120.00	3.32	3.69	2.77
Average					2.81

Table IV. *Competitive formylations*

Initial conc. of reactants in mmoles			Final conc. of products in mmoles		Reactivity relative to I
DMF/POCl ₃	SSe	SS	SSeCHO	SSCHO	K _{XY} /K _{SS}
64.00	66.67	66.67	4.11	0.94	4.48
48.00	50.00	100.00	2.52	1.12	4.59
38.40	40.00	120.00	1.48	0.96	4.69
Average					4.59
	SeSe		SeSeCHO		
64.00	66.67	66.67	10.24	0.79	13.99
48.00	50.00	100.00	5.58	0.80	14.73
38.40	40.00	120.00	3.97	0.88	14.20
Average					14.31

Table V. *Competitive chlorinations*

Initial conc. of reactants in mmoles			Final conc. of products in mmoles		Reactivity relative to I
NCS	SSe	SS	SSeCl	SSCl	K _{XY} /K _{SS}
30.00	33.33	33.33	13.28	3.83	4.16
24.00	25.00	50.00	8.04	4.31	4.30
19.20	20.00	60.00	6.58	5.54	4.12
Average					4.19
	SeSe		SeSeCl		
30.00	33.33	33.33	9.56	1.04	10.66
24.00	25.00	50.00	6.77	1.49	10.44
19.20	20.00	60.00	6.26	2.15	10.29
Average					10.46

Table VI. Competitive acetylations and formylations of II

Initial conc. of reactants in mmoles			Final conc. of products in mmoles			Reactivity relative to α -position in I	
Ac ₂ O	SSe	SS	2-SSeAc	5-SSeAc	2-SSAc	K _{II-2} /K _{I-2}	K _{II-5} /K _{I-5}
64.00	66.67	66.67	3.40	4.35	2.37	1.44	1.86
48.00	50.00	100.00	1.78	2.31	2.46	1.45	1.90
38.40	40.00	120.00	1.21	1.54	2.43	1.50	1.91
Average						1.46	1.89
DMF/POCl ₃	SSe	SS	2-SSeCHO	5-SSeCHO	2-SSCHO		
64.00	66.67	66.67	1.08	3.03	0.47	2.31	6.57
48.00	50.00	100.00	0.67	1.85	0.56	2.40	6.71
38.40	40.00	120.00	0.40	1.08	0.48	2.51	6.83
Average						2.41	6.70

Competitive experiments

In the competitive experiments, all parallel reactions were carried out simultaneously at $25 \pm 0.1^\circ\text{C}$ in a thermostated water-bath. After completion of the reactions, the internal standards were added, the reaction mixtures worked up and analyzed by gas chromatography. The amounts of all products and unreacted starting materials were determined with the help of standard curves, and the reactivity ratios were calculated from the equation given in the text. The results are collected in Tables III–VI, where the same abbreviations as in Table I were used, together with some additional self-explanatory abbreviations needed for the reaction products. In Tables III–V, the final concentrations of the substitution products of selenolo[3,2-b]thiophene (II) given are sums of the concentrations of its 2- and 5-substituted derivatives. These concentrations are instead given in Table VI, where also partial reactivities of position 2 and 5 relative to position 2 in thieno[3,2-b]thiophene (I) are calculated.

In order to limit the consumption of II and III, we ran all competitive reactions at 2.5 times lower concentrations than Bugge's [6]. Furthermore, we did not have to use double internal standards like Bugge, because the differences in retention times of our compounds were not so large. In acetylations, we used 2-formylthieno[3,2-b]thiophene as internal standard; in the formylation of III, we used 2-acetylthieno[3,2-b]thiophene and in the formylation of II we used III, as the retention time of 2-acetylthieno[3,2-b]thiophene turned out to be practically equal to the retention time of 5-formylselenolo[3,2-b]thiophene. In the same way, II was used as an internal standard in chlorinations of III, and III was used in chlorinations of II. All other experimental conditions, such as reaction times, temperatures and work-up procedures, were maintained exactly the same as Bugge's [6].

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References

- Marino, G., *Advan. Heterocycl. Chem.* **1971**, *13*, 235.
- Clementi, S., Fringuelli, F., Linda, P., Marino, G., Savelli, G. and Taticchi, A., *J. Chem. Soc., Perkin II* **1973**, 2097.
- Clementi, S., Fringuelli, F., Linda, P., Marino, G., Savelli, G. and Taticchi, A., *Gazz. Chim. Italiana* **1977**, *107*, 339.
- Litvinov, V. P. and Goldfarb, Ya. L., *Advan. Heterocycl. Chem.* **1976**, *19*, 123.
- Yakushina, T. A., Zvyagintseva, E. N., Litvinov, V. P., Ozolin, S. A., Goldfarb, Ya. L. and Shatenshtein, A. I., *Zhur. Obshch. Khim. SSSR* **1970**, *40*, 1622.
- Bugge, A., *Chemica Scripta* **1972**, *2*, 137.
- Yakushina, T. A., Shapiro, I. O., Zvyagintseva, E. N., Litvinov, V. P., Ozolin, S. A., Goldfarb, Ya. L. and Shatenshtein, A. I., *Zhur. Obshch. Khim. SSSR* **1971**, *41*, 1930.
- Bugge, A., *Acta Chem. Scand.* **1968**, *22*, 63.
- Umezawa, S., *Bull. Soc. Chem. Japan* **1939**, *14*, 363.
- Litvinov, V. P., Konjaeva, I. P. and Goldfarb, Ya. L., "Tezisy Dokladov XIV Nauchn. Sessii po Khim. i Tekhnol. Organich. Soedin. Sery i Sernistych Neftei" p. 196, Riga 1976.
- Russel, G. A., *Competing Reactions, in Technique of Organic Chemistry* (ed. A. Weissberger) Vol. VIII, Part I, p. 358. Interscience, New York 1961.
- Johannesen, R. B., Ferretti, J. A. and Harris, R. K., *J. Magn. Res.* **1970**, *3*, 84.
- Gronowitz, S., Johnson, I. and Bugge, A., *Acta Chem. Scand.* **1976**, *B 30*, 417.
- Gronowitz, S., Konar, A. and Hörnfeldt, A.-B., to be published.
- Gleiter, R., Kobayashi, M., Spanget-Larsen, J., Gronowitz, S., Konar, A. and Farnier, M., *J. Org. Chem.* **1977**, *42*, 2230.
- Litvinov, V. P., Abronin, I. A. and Goldfarb, Ya. L., *Khim. Geterotsikl. Soedin.*, in press.
- Goldfarb, Ya. L., Litvinov, V. P. and Ozolin, S. A., *Izv. Akad. Nauk SSSR* **1968**, 1419.
- Jorgenson, M. J., *Org. Reactions* **1970**, *18*, 1.

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Paper C

^{77}Se NMR Studies of Organoselenium Compounds.

V. Substituent Effects in 2-Substituted Selenolo [3,2-b] selenophenes
Studied by ^1H , ^{13}C and ^{77}Se NMR Spectroscopy.

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V. Substituent Effects in 2-Substituted Selenolo[3,2-b]selenophenes
Studied by ^1H , ^{13}C and ^{77}Se NMR Spectroscopy*

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* For Part IV, see Ref. 1.

Abstract

^{77}Se NMR studies of organoselenium compounds. V. Substituent Effects in 2-substituted selenolo[3,2-b]selenophenes studied by ^1H , ^{13}C and

^{77}Se NMR spectroscopy. Gronowitz, S., Konar, A., Hörnfeldt, A.-B.

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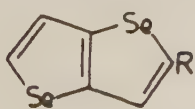
Chemica Scripta (Sweden).

^1H , ^{13}C and ^{77}Se NMR spectra of a series of 2-substituted selenolo[3,2-b]selenophenes have been determined. Derivatives containing both strongly electron-attracting and electron-donating substituents, as well as substituents of intermediate character, were chosen. The substituent-caused chemical shifts are discussed. Comparison with the shifts of the corresponding thieno[3,2-b]thiophenes and selenophenes showed great similarities and good linear correlations were obtained. The influence of substituents on the selenium atoms in both the substituent-bearing and neighbouring rings is discussed. Linear correlations between some of the shifts and dual substituent parameters are also given.

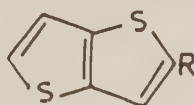
Introduction

In our previous work, the effect of substituents on the ^{77}Se NMR chemical shifts of 2- and 3-substituted selenophenes was studied by the Fourier transform technique [2]. We have also studied arylmethyl-seleno-substituted alkanolic acids, arylmethyl selenides, -diselenides and selenocyanates [3], some methyl- and halo-substituted benzyl- and phenylseleninic acids [1] and 4,4'-disubstituted diphenyl selenides [4]. Very recently Baiwir et al. [5] reported ^{77}Se NMR spectra of [2,3-b]- and [3,2-b]-annelated benzoselenolothiophenes and -selenophenes, and studied the effect of ring fusion and the position of the selenium atom on the ^{77}Se chemical shifts.

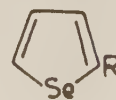
In this connection and in continuation of our work in the selenophene field, we became interested in using the ^{77}Se chemical shifts of 2-substituted selenolo[3,2-b]selenophenes (I) as a probe for studying the interaction between the substituents and the selenium atoms in both the substituent-bearing and neighbouring rings. Thus, in this paper, a comprehensive set of such selenophenes, containing strongly electron-donating, strongly electron-withdrawing substituents and substituents of intermediate character such as methyl and halogens, has been studied by ^1H , ^{13}C and ^{77}Se NMR spectroscopy. Systematic studies of the ^{77}Se NMR spectra of this class of compounds have not previously been reported, although the ^{77}Se NMR spectrum of selenolo[3,2-b]selenophene itself [6], as well as that of its isomers selenolo[2,3-b]selenophene [7] and selenolo[3,4-b]selenophene [8], has been measured.



I



II



III

^1H NMR spectra

In the ^1H , ^{13}C and ^{77}Se NMR measurements, deuterioacetone was used as solvent, TMS as an internal standard and the spectra were recorded at 10 % concentration by weight. The concentration dependence of the chemical shifts was not taken into account, since it was shown by Bugge [9] to be less than 0.02 ppm for the series of 2-substituted thieno[3,2-b]thiophenes (II). All ^1H NMR spectra recorded were either first order or ABX spectra. The assignment of the hydrogens was easily made on the basis of the characteristic ring coupling constants, which fall in well-defined non-overlapping intervals. Furthermore, as the shift difference between α - and β -hydrogens in the unsubstituted selenolo[3,2-b]selenophene in deuterioacetone solution is 0.46 ppm, the β -hydrogens lying at higher field, their relative chemical shifts can be used for complementary assignments. In some cases the refined chemical shift and coupling constant values were obtained iteratively using an extended version of the UEAITR program, the original version of which is given in Ref. 10. The ^1H NMR parameters of the 2-substituted selenolo[3,2-b]selenophenes (I) studied in this work are collected in Table I, where the chemical shifts of all ring hydrogens relative to the parent compound are also given.

^{13}C and ^{77}Se NMR spectra

In the ^{13}C and ^{77}Se measurements deuterioacetone was used as solvent in order to enable use of deuterium as an internal lock signal. The spectra were recorded using the Fourier transform technique and, for ^{77}Se spectra, computer-controlled time averaging of as much as 120000-130000 transients

was required. All shifts were determined from the proton decoupled spectra, using TMS as an internal standard for the ^{13}C and selenophene as an external standard for the ^{77}Se measurements. The ^{13}C chemical shifts were determined with an accuracy of ± 0.2 ppm. The spectra were recorded using the same solutions as the ^1H spectra and the concentration dependence of the shifts was ignored. The ^{13}C NMR spectra of the series of 2-substituted thieno[3,2-b]thiophenes (II) have previously been determined and the principles used for assigning the signals described in detail [11]. Using the same principles in the case of the selenium analogues I, we could ascribe all observed resonances in the ^{13}C spectra. In some cases we have also recorded the undecoupled spectra, in order to be able to compare the coupling constants to those of thieno[3,2-b]thiophenes (II) [11]. The coupling constants and the chemical shifts determined for the compounds studied in this work are given in Table II. In Table III, the chemical shifts of all ring carbon atoms relative to the corresponding carbon atoms in the parent compound are collected.

The ^{77}Se NMR spectrum of selenolo[3,2-b]selenophene was determined previously [6] and showed only one peak at 56.0 ppm upfield from selenophene. The ^{77}Se spectra of all the 2-substituted derivatives determined in this work show two signals, since the two selenium atoms, Se-1 and Se-4, are no longer equivalent. The assignment of these signals was based on comparison with the known substituent-caused ^{77}Se shifts in 2-substituted selenophenes (III) [2] and the ^{77}Se chemical shifts of Se-1 and Se-4 are collected in Table IV,

where the shifts relative to parent selenolo[3,2-b]selenophene are also given. For comparison, the ^{77}Se chemical shifts taken from Ref. 2 of the corresponding 2-substituted selenophenes (III) relative to selenophene are included.

Results and discussion

As mentioned above, the ^1H and ^{13}C NMR spectra of 2-substituted thieno[3,2-b]thiophenes (II) have previously been determined [9,11] and their chemical shifts were shown to correlate very well with the corresponding shifts in 2-substituted thiophenes, as well as with different types of reactivity parameters. Best results were obtained by applying the two-parameter equation of Swain and Lupton [12], which factors the electronic effect of a substituent into resonance and non-resonance components. Because of the success of this treatment, and as, in this way greater insight into substituent effects can be gained, we have in this paper attempted correlations of the various chemical shifts of I with those of the corresponding sulfur analogues II [9,11], with the corresponding derivatives of the monocyclic system III [2,13], as well as with different types of reactivity parameters. The correlation equations are presented in Tables V-VIII and the qualitative aspects of the comparisons are discussed below.

A brief inspection of equations 1-8 given in Table V reveals great similarities between selenophenes I and thiophenes II. This is not surprising considering the structural resemblance of the systems. Replacement of sulfur by selenium in this kind of fused heterocyclic system has recently been shown, by photoelectron spectroscopy of

unsubstituted I and II, as well as of selenolo[3,2-b]thiophene, to be only a minor perturbation, i.e. simple perturbation theory was valid [14]. Excellent correlations ($r > 0.996$) have been found between all three ring hydrogens in I and II (eqns. 1-3). Additionally, all hydrogens also show comparable sensitivity to substituent effects, the slopes of equations 1-3 being very near to 1.00. The same also applies to the ring carbon atoms in I, which correlate well ($r > 0.974$) with the corresponding atoms in II, with the exception of C-6 and C-8. For C-6 an acceptable correlation could, however, be obtained when the substituent CN was excluded from the least-square fit calculations (eqn. 7). Inclusion of the value for CN gave a correlation coefficient of 0.774. The absence of any correlation for C-8 was probably due to the very narrow range of the substituent-caused shifts.

By comparing the ^1H , ^{13}C and ^{77}Se chemical shifts of selenolo[3,2-b]-selenophenes (I) with those of the corresponding selenophenes (III), some information can be obtained concerning the effect of annelation of another ring onto that of selenophene. Results of such comparisons are collated in Table VI. Regarding the ^1H chemical shifts, linear correlations can be obtained for H-3, H-5 and H-6 in I versus H-3, H-5 and H-4 in III, respectively. H-3 in I and III, predictably, give the best correlation (eqn. 9, $r = 0.996$) and show comparable sensitivity to substituent effects, because they are related in a more straight-forward way than the other ring hydrogens. H-5 and H-6, which do not lie in the substituent-bearing ring, show correlations of a somewhat poorer quality (eqns. 10 and 11) and their sensitivity is a half compared to that in the monocyclic ring.

Very good correlations have also been obtained for the ^{13}C shifts of some ring carbon atoms in I and III. The substituent carbon C-2 and the carbon atom ortho to the

substituent C-3, i.e. the atoms in the substituent-bearing ring, give excellent correlations with the corresponding atoms in selenophenes (III) and also show comparable sensitivity to the substituent effect (eqns. 12, 13). Other carbon atoms in I exhibiting good correlations are C-5 and C-7, both of which can be related to C-5 in the corresponding selenophenes (III). The sensitivity of these two carbons to substituent effects is nearly half that of the carbon atoms in the selenophenes, as indicated by the slopes of equations 14 and 15. The corresponding slopes of the equations correlating C-5 and C-7 of thieno[3,2-b]thiophenes (II) with thiophenes were 0.81 and 0.62, respectively. Thus, the difference in efficiency of the transmission of substituent effects over the heteroatom to C-5 and C-7 is greater between I and III than between II and the corresponding thiophenes. Neither C-6 nor C-8 of I can be correlated with any carbon atom in III, a result similar to that obtained when thieno[3,2-b]thiophenes (II) were compared to the corresponding thiophenes [11]. It is therefore somewhat surprising that, as already mentioned, $\Delta H-6$ in I shows a linear correlation, although of poor quality, with $\Delta H-4$ in III (cf. eqn. 11).

The last equation in Table VI shows a linear correlation of high quality between the ^{77}Se chemical shifts of Se-1 in I and ^{77}Se shifts in the corresponding selenophenes (III). These selenium atoms also show comparable sensitivity to substituent effects, indicating that annelation of another selenophene ring does not influence the mode of interaction between substituents and selenium in any appreciable degree. The Se-1 atom shift also exhibits an inverse linear relationship with C-2, having a correlation coefficient of 0.92 (or 0.96 when the value for the iodo-substituted compound was excluded - see below). A similar correlation

was also found between the ^{77}Se and the ^{13}C shifts of the substituent carbon in selenophenes (III) 2. In III, the ^{77}Se shifts also correlate with the shifts at C-3 and C-5, however, no such correlations exist between Se-1 and I and the corresponding carbon atoms.

A brief inspection of Table IV reveals the anomalously small down-field shift of Se-1 in the carbonyl- and nitro- 2-substituted selenophenes (I) as compared to the Se-1 shift in 2-cyanoselenolo[3,2-b]selenophene. This behaviour parallels that observed for the corresponding 2-substituted selenophenes (III) [2]. In order to explain these anomalous shifts, it was suggested that the 2-carbonyl derivatives preferentially exist in the Se-cis form and that their large up-field shift was due to attractive binding interaction between the carbonyl oxygen lone-pair and the selenium d-orbitals, since it could hardly be due to the "normal" anisotropy effect of the carbonyl group on the selenium atom. Similar through-space d-orbital binding can also be operative in 2-nitroselenophene, but must be absent in 2-cyanoselenophene. Considering the above-mentioned Se-1 shifts of 2-carbonyl- and 2-nitro-selenophenes and a very good correlation between Se-1 in I and in III (cf. eqn. 16 in Table VI), it is reasonable to assume that also 2-carbonyl-substituted selenolo[3,2-b]selenophenes exist in Se-cis form and a similar d-orbital - oxygen lone-pair interaction is operative both in these compounds and in 2-nitroselenolo[3,2-b]selenophene.

On the other hand, this effect should not influence the chemical shift of the selenium atom in the neighbouring ring, Se-4, thus no longer outweighing the -M effect of the carbonyl and nitro substituents. Indeed, as the results of Table IV show, this is also the case. Unfortunately, the attempted correlations of the ^{77}Se shifts of this atom with the reactivity parameters, ^1H , ^{13}C or ^{77}Se shifts of III, are of very poor quality. This

can be due to some other effects influencing the Se-4 shift, which we still do not understand sufficiently well or to the fact, that the relatively small range of substituent-caused shifts of this atom results in a rather large relative error. Unfortunately, insufficient quantity of the 2-methoxyselenolo[3,2-b]selenophene prevented recording of its ^{77}Se NMR spectrum and thus extension of the above correlations with this strongly electron-donating substituent was not possible. Since the strong +M character of the methoxy group would give more conclusive information about the sensitivity of Se-4 to substituent effects, we intend to complete this work with the data for the 2-methoxy derivative in the near future.

Correlation with reactivity parameters

A large number of different types of substituent parameters obtained from reactivity data are available [15]. Among various σ_p values, the σ_p^+ values of Swain and Lupton [12] gave best correlations with the ^{77}Se shifts of 4,4'-disubstituted diphenylselenides [4], for which reason these values were also used in this work. The correlations obtained are given in Table VII. The shifts of 2-iodoselenolo[3,2-b]selenophene were excluded from the least-square fit calculations for reasons which were discussed in Ref. 16. Very good linear correlations were obtained for the ^1H shifts of all ring hydrogens and for the ^{13}C shifts of C-5 and C-7. The very poor correlation for C-3 is given for comparison with the

result obtained by applying a two-parameter equation (cf. below). Correlations with the classical Hammett σ_p values [15] were, however, almost as good, while those with σ_p^+ values of Brown and Okamoto [17] were of considerably lower quality. No correlations at all were observed for the C-6 carbon atom. Applying the two-parameter equation of Swain and Lupton [12] did not improve the correlations, but rather decreased the coefficients slightly in all cases except for C-3. Some years ago, Katritzky et al. [18] claimed, from results of infrared measurements, that the trimethylammonium ion group has a resonance donor character, whereas Swain and Lupton had calculated the $\mathcal{R}$ values for the substituents on the assumption that the resonance potential of this ion substituent is negligible in the σ_p series. Although, we are aware of this criticism raised against $\mathcal{F}$ and $\mathcal{R}$ values, we use them in the present work for two reasons. Firstly, we believe that they still can give a qualitative indication of the relative contributions of the inductive and mesomeric effects to the substituent-caused shifts and secondly, since they were used in all our previous studies of substituent effects in selenophenes, we feel it better to continue using them in this work so as to enable comparisons. The original set of field and resonance constants, $\mathcal{F}$ and $\mathcal{R}$, which was calculated for 42 substituents from Hammett's σ_p and σ_m values [12], did not contain parameters for the aldehyde group. Later, Hansch et al. [19] calculated $\mathcal{F}$ and $\mathcal{R}$ values for 191 substituents by a corrected procedure. As this set contains the parameters for CHO-substituent and, since the use of these new $\mathcal{F}$ and $\mathcal{R}$ constants did not alter the values of regression and correlation coefficients to any appreciable degree, we preferred the values of Ref. 19 because of the possibility of

including a greater number of substituents in the regression analysis. Equations 23-28 in Table VIII give the correlations obtained for all three hydrogens and for the carbon atoms in positions 3, 5 and 7. Simple resonance structures, which can be written for I without invoking d-orbital participation of selenium atoms, indicate that for an -I-M substituent the positive charge can be placed on C-3, C-5 or C-7. As seen in Tables VII and VIII, all of these carbons correlate with reactivity parameters, although the correlation for C-3, which is ortho to the substituent, is of poor quality. Bearing in mind the excellent correlations obtained when ^{13}C shifts of selenophenes I were plotted against those of the corresponding thiophenes II (cf. Table V, eqns. 4-8), it is somewhat surprising that no correlation was found for C-3 in II, and moreover, that C-6 in II could be correlated with $\mathcal{F}$ and $\mathcal{R}$ parameters of Swain and Lupton [12] with a correlation coefficient of 0.95 [11]. Otherwise, the comparison of equations 23-25 in Table VIII with the similar equations for the corresponding protons in II [9] and of equations 27 and 28 with the equations for C-5 and C-7 in II [11], reveals great similarities between these two systems, both r and f coefficients being of the same order of magnitude. Comparison of the regression equations obtained for ^1H and ^{13}C chemical shifts in 2-substituted selenophenes (III) [13], again shows great resemblance of H-3 and C-3 in I and III, i.e. atoms in the substituent-bearing ring. Both protons and carbon atoms of the neighbouring ring demonstrate lowered sensitivity to resonance effects, the r -values for H-5 and C-5 in I being 0.76 and 15.2, respectively (see eqns. 24 and 27), compared to the corresponding r -values for H-5 and C-5 in III, 1.99 and 34.0 respectively [13]. This is in perfect agreement with the result of the

equations 10, 11, 14 and 15 in Table VI, where the sensitivity of the corresponding protons and carbon atoms was shown to be one-half of that of the similar atoms in III.

The $\mathcal{F}$ and $\mathcal{R}$ constants of Swain and Lupton [12] are not the only dual substituent parameters (DSP) employed for analysis of spectroscopic data. Topsom [20] has summarized the advantages, which usually offset the disadvantage of increasing the number of adjustable parameters, of such DSP analysis of chemical and spectroscopic data. Triple parameter correlations of substituent-caused shifts in benzene have been reported [21,22] using the parameters $\mathcal{F}$ and $\mathcal{R}$ of Swain and Lupton [12] and the semi-empirical parameter Q . The latter was first introduced by Schaeffer *et al.* [23] in an attempt to account for proximity effects on atoms close to the substituents, and it was suggested that Q might be an empirical measure of the paramagnetic term of the Ramsey equation. Some other triple parameters models have been proposed and are comprehensively treated in a recent review by Ewing [24]. ^{77}Se chemical shifts in 2- and 3-substituted selenophenes gave good single-parameter correlations with Q ($r = 0.971$ and 0.996 , respectively) when the carbonyl and nitro substituents were excluded [2]. However, when these substituents are included the quality of the correlations falls to below 0.85 in both series. Using the full three-parameter regression allows inclusion of all substituents without markedly lowering the quality of the correlation ($r = 0.964$ for 2-substituted and 0.974 for 3-substituted selenophenes), as reported by Smith and Proulx [25]. In the case of 2-substituted selenolo[3,2-*b*]selenophene (I) studied in this work, the simple correlation between Se-1 and Q gives a correlation coefficient of 0.902 and exclusion of the carbonyl and nitro substituents

raises this value to 0.981, probably partly due to the small number of substituents used in the correlation. Using the full three-parameter equation restores r to 0.981, a more satisfying result obviating the elimination of selected data. It should be pointed out in this connection that no correlation could be obtained between Se-1 shifts and $\mathcal{F}$ and $\mathcal{R}$ values, even when the iodo substituent was excluded. Similar results were also obtained for the ^{13}C shift of the substituent carbon atom.

Compounds

Most of the 2-substituted selenolo[3,2-b]selenophenes (I) used in this study were previously unknown and the synthetic approaches to them are presented below. The 2-lithium derivative of selenolo[3,2-b]selenophene is easily obtained by direct metalation with n-butyllithium and this intermediate was used for the preparation of some of the 2-substituted selenophenes I. Thus, carbonation with carbon dioxide gave the carboxylic acid [7], reaction with dimethyl sulphate afforded the 2-methyl derivative, with N,N-dimethylformamide the aldehyde, and with hexachloroethane 2-chloroselenolo[3,2-b]selenophene. The latter two derivatives could also be prepared by electrophilic substitution of the parent selenophene and, in fact, this gave better yields than via the lithium intermediate. Thus, the aldehyde was best prepared by Vilsmeier formylation with the N,N-dimethylformamide - phosphorus oxychloride adduct and the chloro compound by chlorination with N-chlorosuccinimide, analogously to the preparations of the corresponding thieno[3,2-b]thiophene derivatives described by Bugge [26]. The 2-lithium derivative was also used for the preparation of the corresponding boronic acid, which by oxidation with hydrogen peroxide, was hoped to give the

2-hydroxy derivative. The boronic acid was indeed formed but, unfortunately, on oxidation gave only polymeric products. Besides the above-mentioned 2-formyl and 2-chloro derivatives, the 2-acetyl-, 2-iodo- and 2-nitro-substituted compounds were also prepared by the electrophilic substitution of selenolo[3,2-b]selenophene. The 2-acetyl derivative was obtained by Friedel-Crafts acetylation with equivalent amounts of tin(IV) chloride and acetic anhydride in 1,2-dichloroethane [27] and the 2-iodo derivative by the iodine-iodic acid method [28]. The latter was used for the preparation of the 2-methoxy derivative by the copper-promoted reaction with sodium methoxide. In order to obtain the nitro compound, two approaches were used - one by Umezawa, who reported the preparation of 2-nitroselenolo[3,2-b]selenophene in 25 % yield by using nitric acid in acetic anhydride [29], and the other by Bugge, who nitrated thieno[3,2-b]thiophene with copper(II) nitrate trihydrate in acetic anhydride giving the 2-nitro derivative in 54 % yield [26]. In our hands however, both of these procedures gave very low yields of the desired 2-nitroselenolo[3,2-b]selenophene. All of the above-mentioned electrophilic substitution reactions but nitration gave only the 2-substituted compounds; no 3-substitution products could be detected by gas chromatography. However, disubstitution occurred to some extent, giving the 2,5-disubstituted compounds. The 2-cyano derivative was prepared from the aldehyde by the method of Streith et al. [30], using hydroxylamine-O-sulphonic acid in water.

In most of the above-mentioned preparations, the crude reaction product contained varying amounts of the starting material, as detected by GLC, and the required 2-substituted derivatives I were quite difficult to purify by recrystallization. Consequently, in some cases elementary

analyses and melting points are not completely reliable. However, the NMR and mass spectroscopic data were sufficient for establishing beyond doubt the proposed structures.

Experimental

The ^{77}Se NMR spectra were obtained at 19.135 MHz on a Varian XL-100-15 spectrometer equipped with a frequency sweep, a proton wide band decoupler and Fourier transform operation. Field-frequency control (lock) was effected by means of the deuterium resonance of the hexadeuterioacetone. 120,000-150,000 transients were accumulated with a pulse width of 30 μs (flip angle 45°) and a repetition rate of 0.4 s. The shifts were determined from the proton-decoupled spectra with an accuracy of ± 0.2 ppm relative to an external selenophene standard.

The ^{13}C NMR spectra were recorded at 15.04 MHz with a JEOL JNM-60 spectrometer equipped with a built-in JEOL 980 A computer with 12 K memory and the ^{13}C chemical shifts were also determined from the proton-decoupled spectra. The ^1H NMR spectra were obtained with a JEOL MH 100 high resolution spectrometer. Mass spectra were recorded on a Finnigan Model 4021 mass spectrometer and analytical GLC was carried out with a Perkin-Elmer 900 gas chromatograph connected to a Varian 480 digital integrator. The integrator was not calibrated. A Dexil 300 3 % on Chromosorb W AW column was used for all gas chromatographic analyses. For the preparative gas chromatography a Perkin-Elmer F21 preparative instrument equipped with a BDS 20 % on Chrom W column was used. The IR spectra were recorded on a Perkin-Elmer 257 instrument.

Selenolo[3,2-b]selenophene. This compound was obtained as a by-product in the reaction between acetylene and selenium [6] or as described in Ref. 7.

2-Methoxyselenolo[3,2-b]selenophene. To a solution of sodium methoxide, prepared from 0.33 g (0.014 mol) of sodium and 10 ml of abs. methanol, 0.16 g (0.002 mol) of copper(II) oxide and 0.9 g (0.0025 mol) of 2-iodoselenolo[3,2-b]selenophene were added. The reaction mixture was refluxed and followed by gas chromatography during 50 hours. Some decomposition occurred, but the copper salt was filtered off and the methanolic filtrate was poured into water. The water phase was extracted by ether and the combined ether phases were washed with water and dried over magnesium sulphate. During drying and subsequent evaporation the flasks were treated with a minor amount of potassium carbonate. The crude product obtained after evaporation was used for NMR measurements. In the mass spectrum the peaks centred at m/e 266 showed the same pattern as the spectrum simulated for two selenium atoms.

2-Chloroselenolo[3,2-b]selenophene. To a solution of 1.17 g (0.005 mol) of selenolo[3,2-b]selenophene in 50 ml of acetic acid, thermostated to 25°C, 0.67 g (0.005 mol) of N-chlorosuccinimide was added all at once and the reaction mixture was stirred for 24 hours in the dark. After dilution with water the product was extracted with ether and the combined ether phases washed with 2 N sodium hydroxide solution and water and dried over calcium chloride. Evaporation gave 1.36 g of a yellow solid residue. Purification by preparative gas chromatography gave m.p. 51-52°C. In the mass spectrum the peaks centred at m/e 270 showed the same pattern as the spectrum simulated for the two selenium atoms.

2-Iodoselenolo[3,2-b]selenophene. To a mixture of 2.34 g (0.01 mol) of selenolo[3,2-b]selenophene, 3.2 ml of acetic acid, 1.2 ml of water and 10 ml of carbon tetrachloride, three drops of conc. sulphuric acid, 0.82 g of iodine and 0.33 g of iodic acid were added. The reaction mixture was stirred at 40°C for three hours and then cooled to room temperature, whereupon 50 ml of water was added. The water phase was extracted with carbon tetrachloride, the combined organic phases were washed with water, sodium bisulphite and water and dried over calcium chloride. After evaporation of the solvent 1.9 g (52 %) of the title compound was obtained, m.p. 52.5-54°C. In the mass spectrum the peaks centred at m/e 362 showed the same pattern as the spectrum simulated for the two selenium atoms.

2-Methylselenolo[3,2-b]selenophene. To a solution of 7.02 g (0.03 mol) of selenolo[3,2-b]selenophene in 250 ml of dry ether, 24 ml of 1.37 N n-butyllithium in hexane was added dropwise with stirring at room temperature under nitrogen. After refluxing for 20 minutes the reaction mixture was cooled with ice, whereupon 3.65 g (0.03 mol) of dimethyl sulphate in 20 ml of dry ether was added dropwise. Stirring was continued for one hour at room temperature, whereupon 5 ml of saturated ammonium hydroxide solution was added dropwise. After stirring for an additional hour the reaction mixture was poured into ice water. The phases were separated, the water phase was extracted twice with ether and the combined ether phases washed with water, 2 N hydrochloric acid and water and dried over magnesium sulphate. After evaporation, the oily residue obtained was treated with ethanol to give 3.7 g (50 %) of the title compound, m.p. 44-45°C. In the mass spectrum the peaks centred at m/e 250 showed the same pattern as the spectrum simulated for the two selenium atoms.

2-Selenolo[3,2-b]selenophene aldehyde. To a cooled solution of 2.35 g (0.01 mol) of selenolo[3,2-b]selenophene in 16 ml of dimethylformamide, 1.99 g (0.013 mol) of phosphoroxychloride was added with stirring. After stirring for 30 min at 0°C, the reaction mixture was refluxed for 30 min, cooled to room temperature and poured onto ice. After neutralization with 2 N sodium hydroxide solution, the product was extracted with ether and the combined ether phases were washed with diluted sulphuric acid, water, sodium bicarbonate solution and water and dried over magnesium sulphate. Evaporation gave 2.02 g (77 %) of the aldehyde, m.p. 70-72°C. In the mass spectrum the peaks centred at m/e 264 showed the same pattern as the spectrum simulated for two selenium atoms.

2-Acetylselenolo[3,2-b]selenophene and 2-carboxyselenolo[3,2-b]selenophene. These compounds were prepared according to the procedures described in Refs. 27 and 7, respectively.

2-Cyanoselenolo[3,2-b]selenophene. To an inhomogeneous mixture of 1.0 g (0.0038 mol) of 2-selenolo[3,2-b]selenophene aldehyde and 10 ml of water, 0.52 g (0.0046 mol) of hydroxylamine-o-sulphonic acid in 5 ml of water was added dropwise at 30°C. After stirring at this temperature for 15 min the temperature was increased to 65°C for another 30 minutes. After cooling the crystalline product obtained was filtered off and washed with water giving 0.9 g (91 %) of the title compound, m.p. 74-76°C. In the mass spectrum the peaks centred at m/e 261 showed the same pattern as the spectrum simulated for two selenium atoms.

2-Nitroselenolo[3,2-b]selenophene. To a cooled solution of 0.6 g (0.0025 mol) of copper(II) nitrate trihydrate in 9 ml of acetic acid anhydride, 1.17 g (0.005 mol) of selenolo[3,2-b]selenophene in 18 ml of acetic acid anhydride was added dropwise with stirring. During the addition the temperature was kept below 6°C. When the addition was complete the ice-bath was removed and the reaction mixture was stirred at room temperature for 90 min, poured onto ice and left over-night. The mixture was extracted several times with ether and the combined ether phases were washed with 2 N sodium hydroxide solution and water, treated with active carbon and dried over magnesium sulphate. Evaporation gave 0.54 g (39 %) of a yellow solid, m.p. 80-82°C. In the mass spectrum the peaks centred at m/e 281 showed the same pattern as the spectrum simulated for the two selenium atoms.

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References

1. Fredga, A., Gronowitz, S. and Hörnfeldt, A.-B.,
Chemica Scripta 1977, 11, 37.
2. Gronowitz, S., Johnson, I. and Hörnfeldt, A.-B.,
Chemica Scripta 1975, 8, 8.
3. Fredga, A., Gronowitz, S. and Hörnfeldt, A.-B.,
Chemica Scripta 1975, 8, 15.
4. Gronowitz, S., Konar, A. and Hörnfeldt, A.-B.,
Org. Magn. Res. 1977, 9, 213.
5. Baiwir, M., Llabres, G., Piette, J.-L. and Christiaens, L.,
Org. Magn. Res., in press.
6. Gronowitz, S., Frejd, T. and Hörnfeldt, A.-B.,
Chemica Scripta 1974, 5, 236.
7. Gronowitz, S., Konar, A. and Hörnfeldt, A.-B.,
Chemica Scripta 1976, 10, 159.
8. Konar, A. and Gronowitz, S., Tetrahedron, in press.
9. Bugge, A., Chemica Scripta 1973, 3, 190.
10. Johannesen, R.B., Ferretti, J.A. and Harris, R.K.,
J. Magn. Res. 1970, 3, 84.
11. Gronowitz, S., Johnson, I. and Bugge, A., Acta Chem. Scand. 1976, B30,
417.
12. Swain, C.G. and Lupton, E.C., J. Am. Chem. Soc. 1968, 90, 4328.
13. Gronowitz, S., Johnson, I. and Hörnfeldt, A.-B.,
Chemica Scripta 1975, 7, 111.
14. Gleiter, R., Kobayashi, M., Spanget-Larsen, J., Gronowitz, S.,
Konar, A. and Farnier, M., J. Org. Chem. 1977, 42, 2230.

15. Johnson, C.D., The Hammett Equation, Cambridge, 1973.
16. Gronowitz, S., Johnson, I. and Hörnfeldt, A.-B.,
Chemica Scripta 1975, 7, 76.
17. Brown, H.C. and Okamoto, Y., J. Am. Chem. Soc. 1958, 80, 4979.
18. Cutress, N.C., Grindley, T.B., Katritzky, A.R., Sinnott, M.V.
and Topsom, R.D., J. Chem. Soc. Perkin Trans 2 1972, 2255.
19. Hansch, C., Leo, A., Unger, S.H., Hwan Kim, K., Nikaitani, D.
and Lieu, E.J., J. Med. Chem. 1973, 16, 1207.
20. Topsom, R.D., Prog. Phys. Org. Chem. 1976, 12, 1.
21. Berger, S., Tetrahedron 1976, 32, 1451.
22. Smith, W.B., Ihrig, A.M. and Roark, J.I., J. Phys. Chem. 1970, 74, 812.
23. Hruska, F., Hutton, H.M. and Schaefer, T., Can. J. Chem. 1965, 43, 2392.
24. Ewing, D.F., Org. Magn. Res. 1979, 12, 499.
25. Smith, W.B. and Proulx, T.W., Org. Magn. Res. 1976, 8, 567.
26. Bugge, A., Chemica Scripta 1972, 2, 137.
27. Gronowitz, S., Konar, A. and Litvinov, V.P., Chemica Scripta,
in press.
28. Wirth, H.O., Königstein, O. and Kern, W., Ann. 1960, 638, 84.
29. Umezawa, S., Bull. Soc. Chem. Japan 1939, 14, 363.
30. Streith, J., Fizel, C. and Fritz, H., Helv. Chim. Acta 1976, 59, 2786.

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Table I. ^1H NMR chemical shifts (ppm)^a of 2-substituted selenolo-[3,2-b]selenophenes (I) in deuterioacetone solution at 100.0 MHz relative to TMS as an internal standard, and the corresponding protons of unsubstituted selenolo[3,2-b]selenophenes

R	$\delta\text{H-3}$	$\delta\text{H-5}$	$\delta\text{H-6}$	$\Delta\delta\text{H-3}$	$\Delta\delta\text{H-5}$	$\Delta\delta\text{H-6}$	δR
H	7.62	8.08	7.62	0	0	0	-
OCH_3	6.71	7.87	7.42	-0.91	-0.21	-0.20	3.91
Cl	7.57	8.18	7.59	-0.05	0.10	-0.03	-
I	7.92	8.20	7.61	0.30	0.12	-0.01	-
CH_3	7.23	7.96	7.49	-0.39	-0.12	-0.13	2.62
CHO	8.51	8.49	7.79	0.89	0.41	0.17	9.90
COCH_3	8.39	8.40	7.70	0.77	0.32	0.08	2.56
CO_2H	8.39	8.39	7.73	0.77	0.31	0.11	-
CN	8.32	8.48	7.76	0.70	0.40	0.14	-
NO_2	8.67	8.62	7.80	1.05	0.54	0.18	-

^a $\Delta\delta\text{H} = \delta\text{H}(\text{substrate}) - \delta\text{H}(\text{reference})$; positive values are downfield

Table II. ^{13}C NMR chemical shifts (ppm) and direct coupling constants (Hz) of 2-substituted selenolo[3,2-b]selenophenes, in deuterioacetone solution at 15.04 MHz relative to TMS as an internal standard

R	$\delta\text{C-2}$	$\delta\text{C-3}$	$\delta\text{C-5}$	$\delta\text{C-6}$	$\delta\text{C-7}$	$\delta\text{C-8}$	δCH_3	$\delta\text{C=O}$ $\delta\text{C}\equiv\text{N}$	$\text{J}_{\text{C3-H3}}$	$\text{J}_{\text{C5-H5}}$	$\text{J}_{\text{C6-H6}}$
H	131.4	125.8	131.4	125.8	141.3	141.3			170.5	189.0	170.5
OCH_3	171.7	102.9	127.1	128.0	135.5	137.7	61.4				
Cl	132.2	126.1	131.6	126.0	139.6	138.1					
I	75.5	132.0	135.8	125.4	146.8	141.4					
CH_3	147.6	123.9	129.8	125.9	139.4	140.7	18.7				
CHO	150.0	136.7	138.6	126.9	147.6	141.3		185.4	170.9	189.2	174.6
COCH_3	151.0	132.3	137.3	126.8	147.1	141.1	25.6	192.2	169.7	189.8	172.1
CO_2H	147.4	132.5	136.4	126.5	146.8	139.2		164.5			
CN	116.4	137.2	138.2	126.1	147.1	140.1		111.4			
NO_2	154.2	129.6	140.5	126.9	147.8	138.2					

Table III. Chemical shifts (ppm)^a of the carbons of 2-substituted selenolo[3,2-b]selenophenes (I) relative to the corresponding carbons of unsubstituted selenolo[3,2-b]selenophene in deuterioacetone solution

R	$\Delta\delta\text{C-2}$	$\Delta\delta\text{C-3}$	$\Delta\delta\text{C-5}$	$\Delta\delta\text{C-6}$	$\Delta\delta\text{C-7}$	$\Delta\delta\text{C-8}$
H	0	0	0	0	0	0
OCH ₃	40.3	-22.9	-4.3	2.2	-5.8	-3.6
Cl	0.8	0.3	0.2	0.2	-1.7	-3.2
I	-55.9	6.2	4.4	-0.4	5.5	0.1
CH ₃	16.2	-1.9	-1.6	0.1	-1.9	-0.6
CHO	18.6	10.9	7.2	1.1	6.3	0.0
COCH ₃	19.6	6.5	5.9	1.0	5.8	-0.2
CO ₂ H	16.0	6.7	5.0	0.7	5.5	-2.1
CN	-15.0	11.4	6.8	0.3	5.8	-1.2
NO ₂	22.8	3.8	3.1	1.1	5.5	-3.1

^a $\Delta\delta\text{C} = \delta\text{C}(\text{substrate}) - \delta\text{C}(\text{reference})$; positive values are downfield

Table IV. ^{77}Se NMR shifts (ppm)^a of 2-substituted selenolo[3,2-b]-selenophenes (I) and selenophenes (III), in deuterioacetone solution at 19.135 MHz relative to selenophene as an external standard, and the ^{77}Se shifts of I relative to the ^{77}Se absorption of the unsubstituted selenolo[3,2-b]selenophene

R	I				III ^b
	$\delta\text{Se-1}$	$\delta\text{Se-4}$	$\Delta\delta\text{Se-1}$	$\Delta\delta\text{Se-4}$	δSe
H	-56.0	-56.0	0	0	0
Cl	7.5	-31.2	63.5	24.8	41.2
I	64.7	-39.5	120.7	16.5	112.6
CH ₃	-56.9	-41.6	-0.9	14.4	3.8
CHO	-70.8	-26.6	-14.8	29.4	-6.4
COCH ₃	-53.1	-29.6	2.9	26.4	11.7
CO ₂ H	-38.00	-34.00	18.0	22.0	26.2
CN	41.9	-24.6	97.9	31.4	104.3
NO ₂	-42.7	-2.9	7.3	53.1	5.6

^a $\Delta\delta\text{Se} = \delta\text{Se}(\text{substrate}) - \delta\text{Se}(\text{reference})$; positive values are downfield

^b ^{77}Se shifts of 2-substituted selenophenes (III) taken from Ref. 2

Table V. Linear correlations obtained for ^1H and ^{13}C chemical shifts of 2-substituted selenolo[3,2-b]selenophenes (I) versus those of the corresponding 2-substituted thieno[3,2-b]thiophenes (II)^a

	r^b	n^c	
$\Delta\text{H-3} = (1.02 \pm 0.03)\Delta\text{H-3} - (0.12 \pm 0.02)$	0.998	6	(1)
$\Delta\text{H-5} = (0.96 \pm 0.04)\Delta\text{H-5} - (0.04 \pm 0.01)$	0.996	6	(2)
$\Delta\text{H-6} = (0.97 \pm 0.03)\Delta\text{H-6} - (0.06 \pm 0.01)$	0.998	6	(3)
$\Delta\text{C-2} = (1.04 \pm 0.11)\Delta\text{C-2} + (0.03 \pm 1.74)$	0.974	7	(4)
$\Delta\text{C-3} = (1.01 \pm 0.01)\Delta\text{C-3} - (0.07 \pm 0.09)$	0.999	7	(5)
$\Delta\text{C-5} = (0.98 \pm 0.03)\Delta\text{C-5} + (0.16 \pm 0.22)$	0.996	7	(6)
$\Delta\text{C-6} = (0.71 \pm 0.12)\Delta\text{C-6} + (0.14 \pm 0.12)$	0.947	6 ^d	(7)
$\Delta\text{C-7} = (1.18 \pm 0.11)\Delta\text{C-7} - (0.37 \pm 0.47)$	0.983	6 ^e	(8)

^a ^1H shifts taken from Ref. 9; ^{13}C shifts from Ref. 11

^b Correlation coefficient

^c Number of substituents

^d The value for CN was excluded in order to give an acceptable correlation

^e The value for NO_2 was not given in Ref. 11

Table VI. Linear correlations obtained for ^1H , ^{13}C and ^{77}Se chemical shifts of 2-substituted selenolo[3,2-b]selenophenes (I) versus those of corresponding 2-substituted selenophenes (III)^a

	r^b	n^c	
$\Delta\text{H-3} = (0.96 \pm 0.03)\Delta\text{H-3} + (0.12 \pm 0.04)$	0.996	9	(9)
$\Delta\text{H-5} = (0.49 \pm 0.06)\Delta\text{H-5} + (0.15 \pm 0.03)$	0.944	9	(10)
$\Delta\text{H-6} = (0.51 \pm 0.08)\Delta\text{H-4} + (0.08 \pm 0.02)$	0.928	9	(11)
$\Delta\text{C-2} = (0.97 \pm 0.05)\Delta\text{C-2} - (0.60 \pm 1.34)$	0.992	9	(12)
$\Delta\text{C-3} = (0.95 \pm 0.06)\Delta\text{C-3} - (0.16 \pm 0.60)$	0.988	9	(13)
$\Delta\text{C-5} = (0.53 \pm 0.06)\Delta\text{C-5} + (1.10 \pm 0.51)$	0.962	9	(14)
$\Delta\text{C-7} = (0.54 \pm 0.05)\Delta\text{C-5} + (0.18 \pm 0.49)$	0.968	9	(15)
$\Delta\text{Se-1} = (1.07 \pm 0.09)\Delta\text{Se} - (3.18 \pm 5.28)$	0.978	8	(16)

^a ^1H and ^{13}C shifts of III taken from Ref. 12; ^{77}Se shifts from Ref. 2

^b Correlation coefficient

^c Number of common substituents

Table VII. Linear correlations obtained for ^1H and ^{13}C chemical shifts of 2-substituted selenolo[3,2-b]selenophenes versus the σ_p^+ values of Swain and Lupton [12].

	r^a	n^b	
$\Delta\text{H-3} = (1.37 \pm 0.09)\sigma_p^+ - (0.03 \pm 0.05)$	0.989 (0.870)	7	(17)
$\Delta\text{H-5} = (0.52 \pm 0.04)\sigma_p^+ + (0.07 \pm 0.02)$	0.982 (0.979)	7	(18)
$\Delta\text{H-6} = (0.27 \pm 0.02)\sigma_p^+ - (0.04 \pm 0.01)$	0.989 (0.984)	7	(19)
$\Delta\text{C-3} = (19.0 \pm 4.28)\sigma_p^+ - (3.74 \pm 2.31)$	0.893 (0.827)	7	(20)
$\Delta\text{C-5} = (9.23 \pm 0.67)\sigma_p^+ + (0.93 \pm 0.36)$	0.987 (0.945)	7	(21)
$\Delta\text{C-7} = (9.00 \pm 0.95)\sigma_p^+ - (0.15 \pm 0.51)$	0.973 (0.870)	7	(22)

^a Correlation coefficient; figures in parentheses reflect r-values obtained with inclusion of I substituent

^b Number of substituents not including the iodo derivative

Table VIII. Regression equations relating ^1H and ^{13}C chemical shifts of 2-substituted selenophenes (I) to substituent constants, $\mathcal{F}$ and $\mathcal{R}_a$

	$\frac{b}{\sigma}$	r_c	n_d
$\Delta\text{H-3} = (0.05 \pm 0.17) + (0.96 \pm 0.42)\mathcal{F} + (2.24 \pm 0.64)\mathcal{R}$	0.21	0.949	9 (23)
$\Delta\text{H-5} = (0.02 \pm 0.04) + (3.56 \pm 0.11)\mathcal{F} + (0.76 \pm 0.17)\mathcal{R}$	0.06	0.974	9 (24)
$\Delta\text{H-6} = -(0.04 \pm 0.03) + (0.24 \pm 0.08)\mathcal{F} + (0.43 \pm 0.12)\mathcal{R}$	0.04	0.952	9 (25)
$\Delta\text{C-3} = (3.51 \pm 3.21) - (5.41 \pm 8.34)\mathcal{F} + (43.5 \pm 11.7)\mathcal{R}$	4.08	0.928 (0.815)	8 (26)
$\Delta\text{C-5} = (0.86 \pm 1.02) + (7.51 \pm 2.66)\mathcal{F} + (15.2 \pm 3.71)\mathcal{R}$	1.30	0.963 (0.925)	8 (27)
$\Delta\text{C-7} = (1.60 \pm 1.01) + (2.15 \pm 2.62)\mathcal{F} + (17.7 \pm 3.66)\mathcal{R}$	1.28	0.963 (0.825)	8 (28)

$\frac{a}{\text{—}}$ $\mathcal{F}$ and $\mathcal{R}$ values of Ref. 19

$\frac{b}{\text{—}}$ Standard deviation in ppm

$\frac{c}{\text{—}}$ Correlation coefficient; figures in parentheses reflect r values obtained with inclusion of I substituent

$\frac{d}{\text{—}}$ Number of substituents in the regression analysis not including the iodo derivative

Paper D

On the Electronic Effects of the Heteroatom in Five-Membered Heterocycles. Photoelectron Spectra of Selenolo and Pyrrolo Analogues of Thieno [2,3-b] - thiophene and Thieno [3,2-b] thiophene.

On the Electronic Effects of the Heteroatom in Five-Membered Heterocycles. Photoelectron Spectra of Selenolo and Pyrrolo Analogues of Thieno[2,3-*b*]thiophene and Thieno[3,2-*b*]thiophene¹

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In order to study the effects of the heteroatoms, the photoelectron spectra of thieno[2,3-*b*]selenophene (3), selenolo[2,3-*b*]selenophene (4), thieno[3,2-*b*]selenophene (5), selenolo[3,2-*b*]selenophene (6), thieno[2,3-*b*]pyrrole (7), selenolo[2,3-*b*]pyrrole (8), pyrrolo[2,3-*b*]pyrrole (9), thieno[3,2-*b*]pyrrole (10), and selenolo[3,2-*b*]pyrrole (11) have been measured and analyzed. Replacement of sulfur by selenium can be considered as a minor perturbation, i.e., simple perturbation theory is valid. The effect on the π electronic system of a replacement of sulfur or selenium by an NH group is governed by a balance between the influence of the increase of the resonance integral for the bonds involving the heteroatom and a strongly destabilizing inductive effect due to the polarity of the N-H bond. The effective electronegativity of the NH group is found to be not too different from that of a sulfur atom.

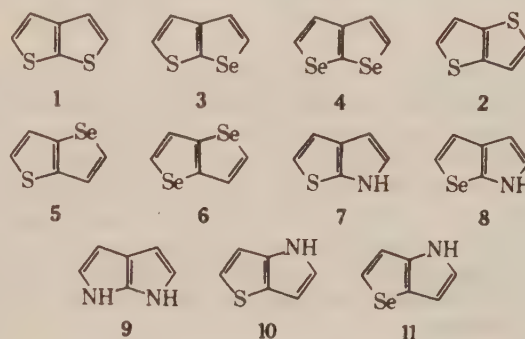
A description of the electronic effects associated with the heteroatom in a heterocyclic compound is of fundamental importance in chemistry and biology. Heterocyclic chemistry is a rich field for the application of perturbation theoretical arguments, and qualitative descriptions of the influence of the heteroatom are in most cases based directly or indirectly on simple perturbation theory.⁵ A prominent example of a series of heterocycles is the compounds C_4H_4X , where X may be O, S, Se, NH, etc. In Figure 1 we have indicated the positions of the first two ionization potentials^{6,7} of the compounds furan, pyrrole, thiophene, and selenophene, arranged in the order of decreasing electronegativity of the heteroatom. Within the validity of Koopmans' theorem (see later), the first and the second ionization potential correspond to removal of an electron from the highest and the second highest molecular orbital, $a_2(\pi)$ and $b_1(\pi)$, respectively. The general shape of these orbitals is indicated below. According to simple per-



turbation theory, the energy of the $a_2(\pi)$ level should be much less affected by a change of heteroatom than the energy of the $b_1(\pi)$ level. Inspection of Figure 1 shows that this expectation holds excellently for the series furan, thiophene, and selenophene, but pyrrole is a striking exception. Consider for instance the passing from thiophene to pyrrole: the shift of the $a_2(\pi)$ level is much larger than the shift of the $b_1(\pi)$ level, and both shifts are toward lower binding energies, which is apparently inconsistent with an increase of electronegativity of the heteroatom.

In order to obtain a better understanding of the effects operating in these systems, we have studied the PE spectra of thieno[2,3-*b*]selenophene (3),⁸ selenolo[2,3-*b*]selenophene (4),⁹ thieno[3,2-*b*]selenophene (5),¹⁰ selenolo[3,2-*b*]selenophene (6),¹¹ thieno[2,3-*b*]pyrrole (7),¹² selenolo[2,3-*b*]pyrrole (8),¹³ pyrrolo[2,3-*b*]pyrrole (9),¹³ thieno[3,2-*b*]pyrrole (10),¹³ and selenolo[3,2-*b*]pyrrole (11).¹³ The PE spectra of thieno[2,3-*b*]thiophene (1) and thieno[3,2-*b*]thiophene (2) have been measured previously.¹⁴

In the first section of the paper we discuss the compounds 1-6, where simple perturbation theoretical arguments appear to be valid. In the second and largest part of the paper we discuss the compounds 7-11 in order to describe the effects leading to the breakdown of simple perturbation theory when



sulfur or selenium is replaced by NH. We use the results of current semiempirical methods and refer to recent *ab initio* results, but the emphasis has been put on a conceptual analysis in terms familiar to most organic chemists.

1. PE Spectra of 1-6

The PE spectra of 3-6 are shown in Figure 2 and the vertical ionization potentials of the first four bands are listed in Table I. The PE spectra of 1 and 2 have been published previously,¹⁴ and the vertical ionization potentials are included in Table I. The PE spectra of the series 1-3-4 all look very similar, as do the PE spectra of the series 2-5-6. This is not surprising, since sulfur and selenium have very similar electronegativities,¹⁵ and substitution of sulfur by selenium can be expected to be a minor perturbation of the valence electronic system. In the following section is given a more detailed discussion of this matter in connection with a description of the effects due to the NH group.

In our interpretation of these spectra we assume the validity of Koopmans' theorem.¹⁶ In this approximation, the negative value of the orbital energy, ϵ_J , is set equal to the vertical ionization potential, $I_{V,J}$:

$$-\epsilon_J = I_{V,J} \quad (1)$$

As in the case of 1 and 2¹⁴ we take the steep onset of the first few PE bands as an indication that the bands correspond to ionizations from π orbitals. From the similarity of the PE spectra mentioned above, the correlation diagram given in Figure 3 can be drawn. To check this diagram we have carried out semiempirical calculations using a parametrized Hückel (HMO) procedure,⁵ and the EWMO,^{17,18} CNDO/2,¹⁹ and MINDO/3²⁰ methods. The results of the HMO and MINDO/3 calculations are summarized in Table I, and a correlation diagram based on the HMO results is presented in Figure 4.

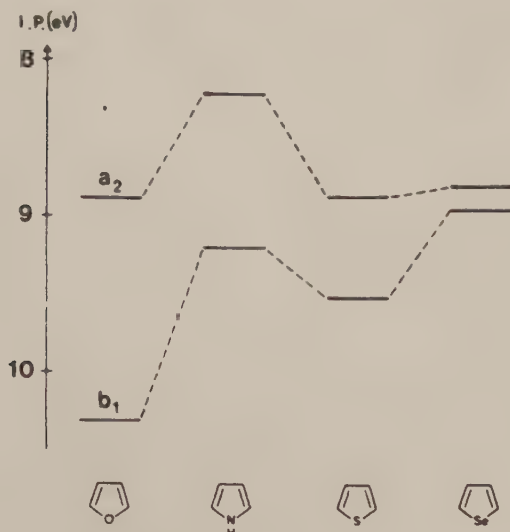


Figure 1. Correlation of the observed first and second ionization potentials of the compounds furan, pyrrole, thiophene, and selenophene.

HMO Model. The parameters for the HMO calculations were chosen in a straightforward way. α_X and β_{CX} values for $X = S$ and Se were taken as those used previously: $\alpha_S = -9.4$, $\alpha_{Se} = 8.5$, $\beta_{CS} = -1.8$, and $\beta_{CSe} = -1.5$ eV.²¹ The β_{CC} value was also kept in accordance with the previous work: $\beta_{CC} = -3.0$ eV.²¹ The α_C value was then adjusted to reproduce the observed first ionization potential of thiophene (8.87 eV⁶) and selenophene (8.80 eV⁷). The HOMOs of these compounds have a node through the position of the heteroatom X , and are thus independent of the choice of α_X and β_{CX} parameters in

the HMO model. A good agreement is found for $\alpha_C = -7.0$ eV, which yields a common value of -8.85 eV for the energies of these levels. The results for thiophene and selenophene are then (eV)

	Thiophene	Selenophene
$a_2(\pi)$	-8.85	-8.85
$b_1(\pi)$	-9.64	-8.93
$b_1(\pi)$	-12.56	-12.23

The agreement with the observed energies^{6,7} is satisfactory; in particular, the consistency with the recent analysis of the PE spectrum of thiophene by Niessen et al.²² is gratifying.

Results and Discussion. The results of the HMO calculations on the compounds 1–6 agree reasonably well with the experimental energies; see Table I. The results support the assignments suggested previously¹⁴ for 1 and 2; this assignment is furthermore supported by the MINDO/3 results for 1 and 2 given in Table I. Comparison of the correlation diagrams in Figures 3 and 4 shows that the HMO calculations reproduce the significant trends in the PE spectra for this series of compounds. Most of the observed shifts of the bands can be understood in terms of simple first-order perturbation theory applied to the HMOs of 1 and 2 (see Figure 4). The HOMO of 1 has a small amplitude on the sulfur atoms, while the next MO has a large amplitude in these positions. These orbitals are thus destabilized to different extents by replacement of sulfur by selenium, and a reversal of the ordering of these two closely spaced levels is predicted in the series 1–3–4. Similar shifts are shown by the two highest occupied orbitals in 2, which have the same symmetry (a_u in C_{2h}). At first glance it may appear strange that the energy of the second highest MO approaches the energy of the HOMO in the series

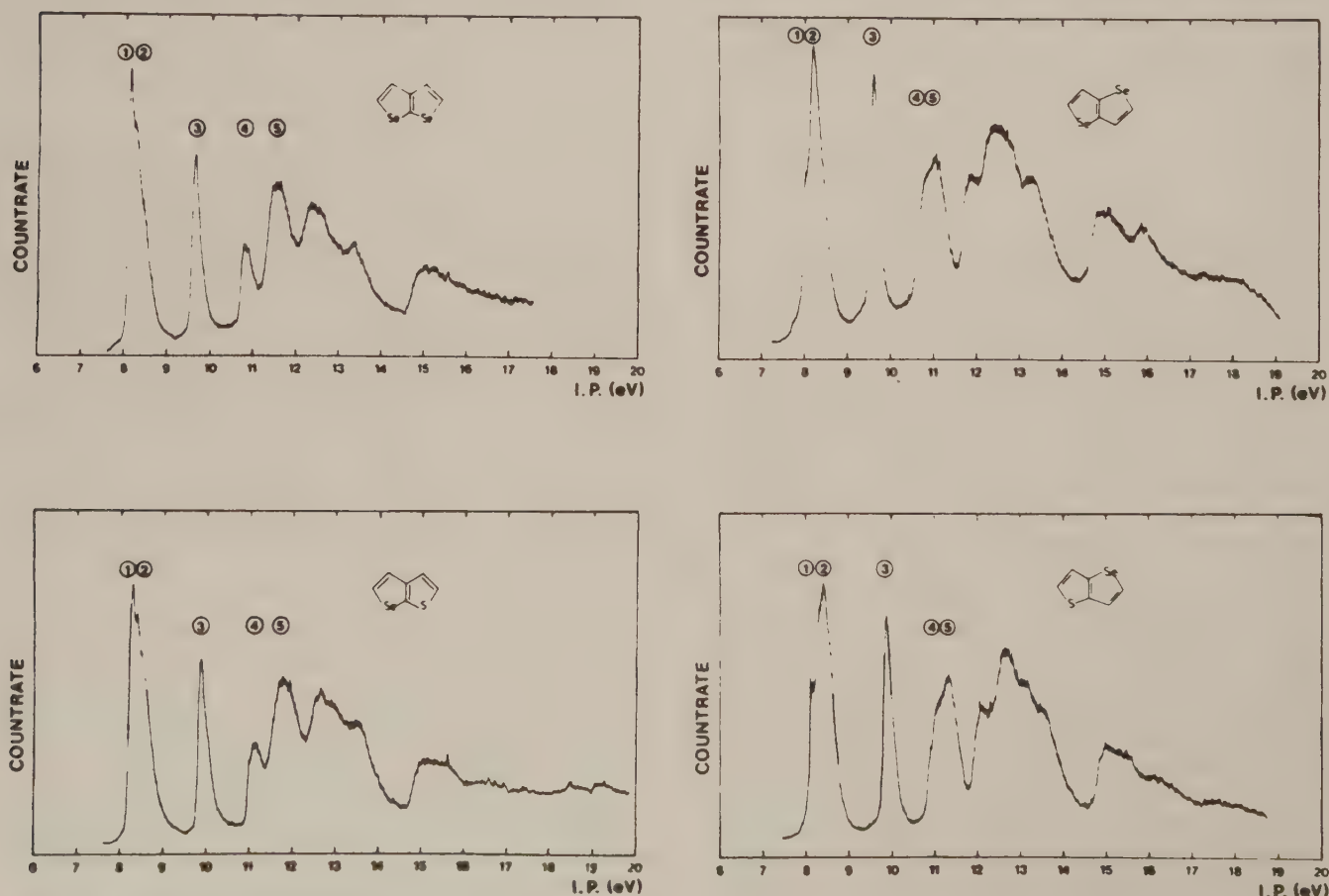


Figure 2. PE spectra of the compounds 3–6.

Table I. Measured Vertical Ionization Potentials, $I_{V,J}$, and Orbital Energies, ϵ_J , for 1–6. All Values in eV

Registry no.	Compd	Band	$I_{V,J}^a$	Assignment ^a	ϵ_J (HMO)	ϵ_J (MINDO/3) ^b
250-84-0	1 (C_{2v})	①	8.32	4b ₁ (π)	-8.48	-8.27
		②	8.41	3a ₂ (π)	-8.60	-8.47
		③	10.08	3b ₁ (π)	-10.28	-9.76
		④	11.27	2a ₂ (π)	-11.10	-11.50
23787-71-5	3 (C_s)	①	8.28	8a'' (π)	-8.32	
		②		7a'' (π)	-8.49	
		③	9.88	6a'' (π)	-9.87	
		④	11.12	5a'' (π)	-10.91	
250-85-1	4 (C_{2v})	①	8.16	4a ₂ (π)	-8.16	
		②		5b ₁ (π)	-8.45	
		③	9.66	4b ₁ (π)	-9.51	
		④	10.82	3a ₂ (π)	-10.59	
251-41-2	2 (C_{2h})	①	8.10	4a _u (π)	-8.25	-8.15
		②	8.61	3a _u (π)	-8.94	-8.57
		③	10.04	3b _g (π)	-10.25	-9.67
		④	11.5	2b _g (π)	-11.11	-11.53
		⑤		15a _g (σ)		-9.33
20503-37-1	5 (C_s)	①	8.08	8a'' (π)	-8.19	
		②	8.39	7a'' (π)	-8.61	
		③	9.86	6a'' (π)	-9.97	
		④	11.3	5a'' (π)	-10.93	
		⑤		32a' (σ)		
251-49-0	6 (C_{2h})	①	8.05	5a _u (π)	-8.09	
		②	8.20	4a _u (π)	-8.50	
		③	9.63	4b _g (π)	-9.47	
		④	11.1	3b _g (π)	-10.84	
		⑤		18a _g (σ)		

^a The ionization potentials and assignments reported for 1 and 2 are taken from ref 14. ^b Some σ orbitals between the π orbitals have been omitted. The calculations were based on geometries derived from the experimental structure of thiophene; see ref 25.

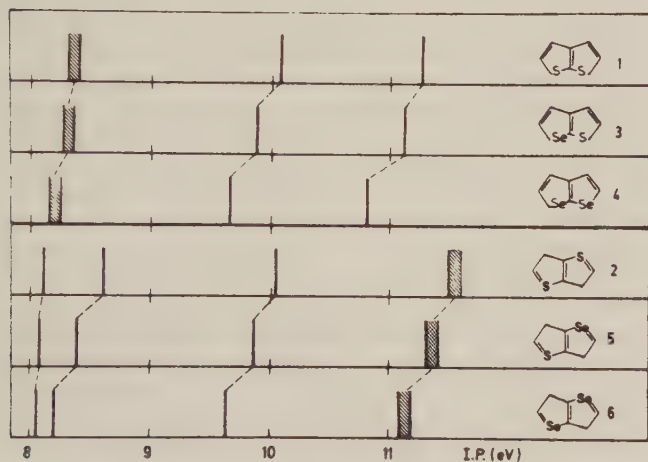


Figure 3. Correlation of the observed first four ionization potentials in the series 1–3–4 and 2–5–6; see Table I.

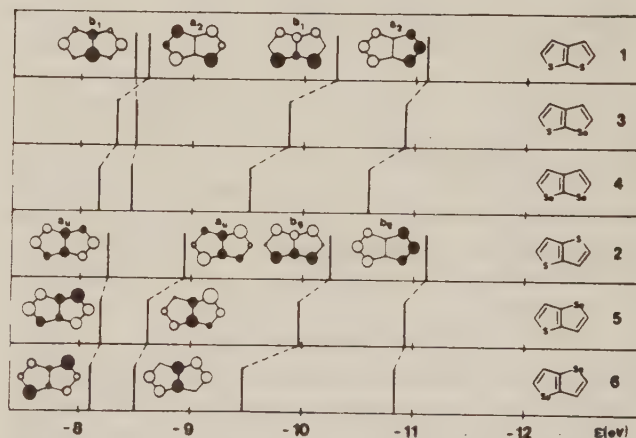
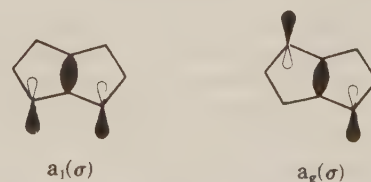


Figure 4. Correlation of the calculated energies of the four highest occupied HMO levels for the series 1–3–4 and 2–5–6; see Table I. The shape of the most important orbitals is indicated schematically.

2–5–6 without shifting the latter much. The shapes of the orbitals shown in Figure 4, however, indicate that the interaction is considerable, corresponding to the initial stages of an avoided crossing.

We finally briefly mention a few results regarding the highest occupied σ level in these compounds. According to the results of an extended Hückel calculation reported previously,¹⁴ the highest occupied σ orbital in 1 and 2 transforms according to A_1 and A_g , respectively. The corresponding amplitudes are indicated schematically below.

These results are confirmed by the CNDO/2 and MINDO/3 methods, and by the results of EWMO calculations for 1–6. The calculations predict a destabilization of the $a_g(\sigma)$ orbital



relative to the $a_1(\sigma)$ orbital due to a very strong antibonding interaction between the n_+ "lone pair" combination and the central C–C σ bond in the series 2–5–6. Our assignment of the overlapping bands ④ and ⑤ in the spectra of this series of compounds to ionization out of a π and a σ level is consistent with this result.

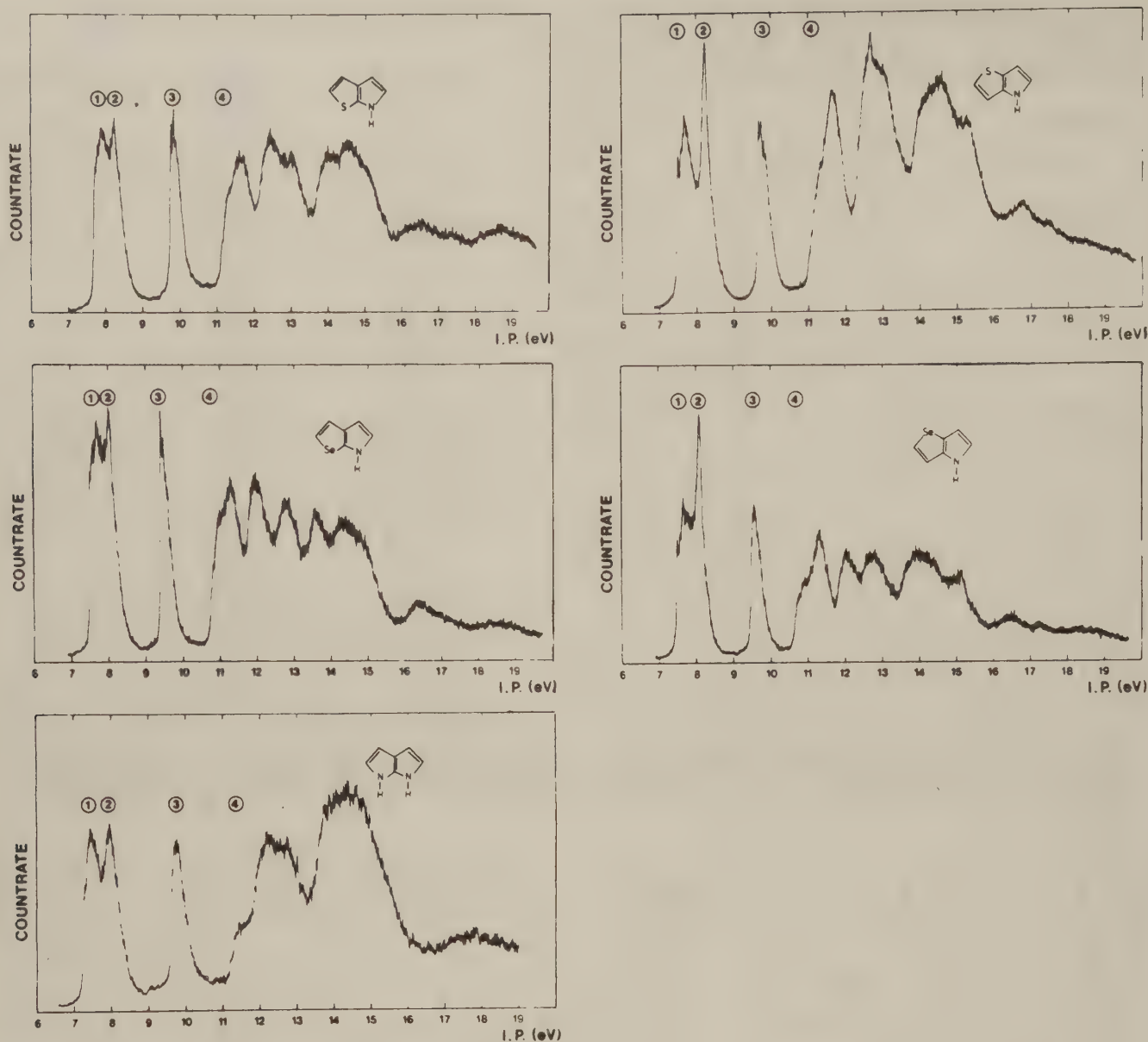


Figure 5. PE spectra of the compounds 7-11.

II. PE Spectra of 7-11

Replacement of sulfur or selenium in the compounds 1-6 by an NH group yields the compounds 7-11. The PE spectra of these compounds are shown in Figure 5, and the vertical ionization potentials are given in Table II. The assignment of the first broad peak in the spectra of the compounds 1-6 to two overlapping transitions (band ① and ②) is immediately supported by the comparison with the spectra of 7-11: the peak is clearly split into two components.

Electronic Effects of the NH Group. The discussion of the PE spectra of 1-6, was simplified by the circumstance that replacement of sulfur by selenium can be considered as a minor perturbation. Replacement of sulfur or selenium by an NH group, however, is not a small perturbation, and simple perturbation theory is no longer valid. As indicated in the introduction, this is easily seen by a comparison of the PE spectrum of pyrrole with the PE spectra of thiophene and selenophene (see Figure 1). Usual π electron theory will fail to describe this phenomenon properly, since the dominant interactions in pyrrole take place through the σ system; while the pyrrole nitrogen is a π electron donor, it is a much stronger σ electron acceptor.²³ An all-valence electron model with in-

clusion of electron interaction terms is appropriate for an understanding of these effects. In closed-shell SCF theory the orbital energy ϵ_J can be considered as a sum of two terms,²⁴

$$\epsilon_J = H_{JJ} + \sum_K (2J_{JK} - K_{JK}) = H_{JJ} + G_{JJ} \quad (2)$$

where the summation is over the occupied orbitals. The first term, H_{JJ} , represents the kinetic energy of an electron in the orbital J plus its potential energy due to the attraction by the nuclei. The second term, G_{JJ} , represents an average value of the repulsion between the electron in the orbital J and all other electrons in the molecule. The orbital energy ϵ_J is thus the sum of two large contributions with opposite sign.

Consider now the HOMO of furan, $a_2(\pi)$. This orbital is localized in the butadiene fragment with zero amplitude on the heteroatom, as mentioned before (see Figure 6). Replacing the oxygen atom by a sulfur atom or an NH group leads to an increase of H_{JJ} and a decrease of G_{JJ} for this orbital, as illustrated in the top of Figure 6 where the results of a CNDO/2 calculation are shown. This can be explained by the change of geometry taking place;²⁵ part of the attracting core, as well as part of the repulsing electron density, is moved away from the region of the $a_2(\pi)$ orbital. The shifts are particularly large

Table II. Measured Vertical Ionization Potentials, $I_{V,J}$, and Orbital Energies, ϵ_J , for 7–11. All Values in eV

Registry no.	Compd	Band	$I_{V,J}$	Assignment	ϵ_J (HMO)	ϵ_J (MINDO/3) ^a
250-79-3	7 (C _s)	①	7.97	6a'' (π)	-7.99	
		②	8.31	5a'' (π)	-8.11	
		③	9.89	4a'' (π)	-10.09	
		④	11.45	3a'' (π)	-11.30	
42425-03-6	8 (C _s)	①	7.74	7a'' (π)	-7.89	
		②	8.09	6a'' (π)	-8.04	
		③	9.48	5a'' (π)	-9.53	
		④	11.13	4a'' (π)	-11.16	
58326-34-4	9 (C _{2v})	①	7.46	2a ₂ (π)	-7.60	-7.53
		②	7.91	3b ₁ (π)	-7.97	-7.51
		③	9.73	2b ₁ (π)	-9.96	-9.61
		④	11.47	1a ₂ (π) 16a ₁ (σ)	-11.33	-11.89 -10.11
250-94-2	10 (C _s)	①	7.70	6a'' (π)	-7.81	
		②	8.24	5a'' (π)	-8.41	
		③	9.66	4a'' (π)	-9.97	
		④	11.3	3a'' (π)	-11.24	
58326-29-7	11 (C _s)	①	7.67	7a'' (π)	-7.77	
		②	8.10	6a'' (π)	-8.22	
		③	9.60	5a'' (π)	-9.66	
		④	10.95	4a'' (π)	-10.88	

^a Some σ orbitals between the π orbitals have been omitted. The geometry of 9 was derived from the experimental geometry of pyrrole; see ref 25.

in going from furan to thiophene; the decrease of G_{JJ} , however, is found to practically compensate the increase of H_{JJ} , so that the orbital energy ϵ_J stays constant; see the bottom of Figure 6. This can be observed throughout the series furan, thiophene, selenophene, and tellurophene.^{6,7,26} In the case of going from furan to pyrrole the increase of H_{JJ} is found to be larger than the decrease of G_{JJ} , leading to a net destabilization of the $a_2(\pi)$ level; see Figure 6. This is a direct consequence of the high polarity of the N–H bond, which tends to increase the G_{JJ} value by increasing the electron density in the ring: ab initio Hartree–Fock calculations^{22,27} show that the total excess charge on the five ring atoms is ca. 25% larger in pyrrole than in furan or thiophene. Substitution of the NH hydrogen atom by an electron-donating methyl group leads to further destabilization of the $a_2(\pi)$ level.^{28,29} We may thus summarize that although the individual shifts of H_{JJ} and G_{JJ} are much larger in the case of going from furan to thiophene than in the case of going from furan to pyrrole,³⁰ the destabilizing and stabilizing effects tend to cancel in the first case, but not in the second case.

We then turn briefly to the second highest occupied orbital in these compounds, $b_1(\pi)$. This orbital has a high amplitude on the heteroatom and it would appear reasonable to expect that the shifts of this level can be predicted by simple perturbation theory. One would thus predict a stabilization of this level when the heteroatom is replaced by a more electronegative atom. Calculated^{22,27} and observed (Figure 1) energies support this prediction in the case of going from thiophene to furan, but not in the case of going from thiophene to pyrrole. The calculations by Niessen et al.^{22,27} predict essentially the same energy of this orbital in thiophene and pyrrole, and the measured binding energies show a destabilization of 0.3 eV of the level in pyrrole relative to the level in thiophene (see Figure 1); the increase in electronegativity of the heteroatom is thus not able to outweigh the destabilizing inductive effect discussed in the preceding paragraph. This is largely due to the circumstance that although nitrogen is clearly more electronegative than sulfur,¹⁵ the effective electronegativity of the NH group is probably not too different from that of a sulfur atom. The nitrogen atom in pyrrole gains approximately

0.4 electron, but ca. three-quarters of that is withdrawn from the hydrogen atom bonded to it;²⁷ the capacity to withdraw electrons from the neighboring carbon atoms is thus strongly deactivated, and the effective electronegativity of the NH group is much less than that of the nitrogen atom.

Contrary to the two highest occupied orbitals discussed above, $a_2(\pi)$ and $b_1(\pi)$, the third and most bonding π orbital in these compounds has large C–X bond contributions, and is thus quite sensitive to the strength of this π bond as measured by the value of the resonance integral β_{CX} . In the case of going from thiophene to furan, the large stabilizing effect due to the large magnitude of β_{CO} relative to β_{CS} cooperates with the increase of electronegativity of the heteroatom to yield a very large stabilization of the third π level, ca. 3 eV.²² When passing from thiophene to pyrrole, it turns out that the stabilizing effect due to the bond contributions dominates over the destabilizing inductive effect of the NH group, and the level is stabilized by ca. 1 eV.^{22,27} In this paper, however, we deal primarily with levels related to the two first π orbitals, $a_2(\pi)$ and $b_1(\pi)$.

So far we have not considered the effects due to a possible deviation from Koopmans' approximation (1). Niessen et al.^{22,27} have recently calculated "Koopmans' defects" for furan, pyrrole, thiophene, and others, by means of highly sophisticated many-body perturbation theory. They obtained very small corrections for the $a_2(\pi)$ levels, in agreement with the close correspondence between calculated ab initio orbital energies and measured ionization potentials shown in Figure 6. This means that the analysis based on (2) is valid. The corrections obtained for the inner π levels were not negligible, but the shifts of the calculated ionization potentials were in all cases well predicted by the shifts of the corresponding orbital energies. This indicates that a description of the trends in the PE spectra of these compounds in terms of MO theory is reasonable.

HMO Model. The discussion given in the preceding paragraph of this section attempts to explain why the effects of replacement of sulfur or selenium atoms in compounds like 1–6 by NH groups cannot be described by simple perturbation theory. Any reasonable model must include the large inductive

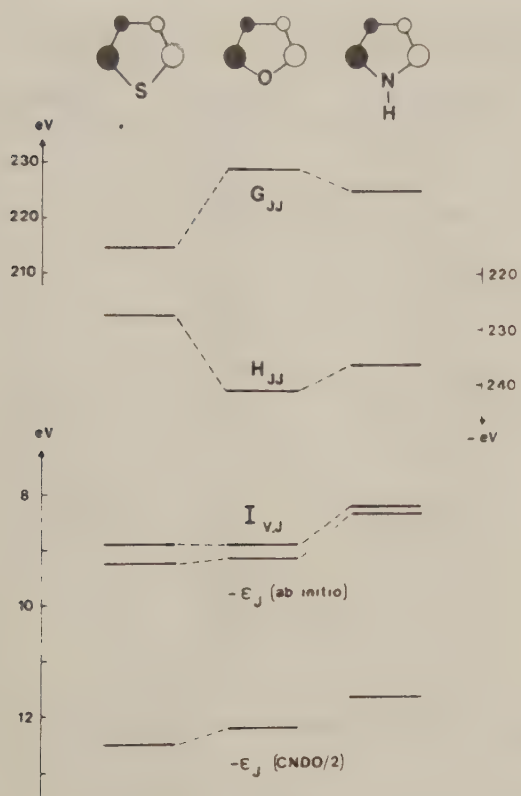


Figure 6. Top: Correlation of the calculated values of H_{JJ} and G_{JJ} (see the text) for the $a_2(\pi)$ orbitals in thiophene, furan, and pyrrole. The results were obtained by the CNDO/2 method and are based on the experimental geometries given in ref 25. Note that the values for H_{JJ} are negative. Bottom: Correlation of the measured ionization potentials I_{VJ} and of the calculated orbital energies $\epsilon_J = H_{JJ} + G_{JJ}$ for the $a_2(\pi)$ levels in thiophene, furan, and pyrrole. The *ab initio* results are taken from ref 22 and 27; the CNDO/2 results correspond to the results mentioned above.

effect of the NH group on the carbon frame. Eland⁶ has proposed a parametrization of the HMO model which leads to good agreement with the first few PE bands of pyrrole, indole, and aniline. This parametrization employs α_C values of smaller magnitude than the value -7.0 eV derived for thiophene and selenophene in the preceding section: $\alpha_C = -6.37$ eV and $\alpha_C^{\text{adj}} = \alpha_C - 0.27$ eV.³¹ This is consistent with the destabilizing tendency described above (Elands's choice was not based on this argument, however; he was unable to obtain a good agreement for thiophene). The remaining parameters proposed by Eland are $\beta_{CC} = \beta_{CN} = -2.70$ eV and $\alpha_N = \alpha_C + \beta_{CC} = -9.07$ eV. It is interesting to note that this α_N value is not very different from the value -9.4 eV obtained for α_S ,²¹ indicating that the effective electronegativities are in fact quite similar (see also ref 5c, p 127).

We have performed a calculation using Eland's parameters on pyrrolo[2,3-*b*]pyrrole (9), and the results are in good agreement with experiment; see Table II.³² We take this as an indication that the parametrization may be adequate for the series 7–11. We apply Eland's parameters in the following way: for all atoms and bonds in a pyrrole fragment in 7–11 we use Eland's values, and in the remaining portions we keep the parameters derived in the previous section. It should be noted that the parameters lead to an underestimation of the binding energy of the third π level in the PE spectrum of pyrrole (~ 13.7 eV²⁷); accordingly, we limit our attention primarily to the first three levels in 7–11 which are related to the first two levels in pyrrole.

Results and Discussion. The results of the calculations are listed in Table II, where also the results of a MINDO/3

calculation on 9 are included. The comparison of the observed and calculated energies shows that the HMO model, being pushed that far, is able to yield a very reasonable agreement with experiment. A correlation diagram of the first three PE bands in the series of [2,3-*b*]-fused compounds 1, 7, 9, 8, and 4 is presented in Figure 7, and the corresponding diagram based on the HMO results is given in Figure 8. It is apparent that a number of significant trends are reproduced by the calculation, as discussed in the following. Successive replacement of sulfur atoms in 1 by NH groups to yield 7 and 9 is predicted to lead to a destabilization of the three highest occupied π levels, consistent with the destabilization of the two highest occupied π levels of pyrrole relative to the corresponding levels in thiophene. This is due primarily to the general shift toward lower binding energies introduced by the use of smaller α_C magnitudes for the pyrrole fragments. The two highest occupied near-degenerate π levels of 1 are predicted to experience very different shifts, leading to a considerable split of the levels as observed in the PE spectra (Figures 5 and 7). The a_2 level is destabilized more than the b_1 level, which means that the order is being reversed in the series 1–7–9. A similar crossing was predicted in the series 1–3–4 (see Figure 4), although mainly for a different reason. The different shifts of the two levels are in the present case largely due to the difference in C–X bonding characteristics; the C–X bond contributions of the b_1 orbital are small and tend to cancel, while the a_2 orbital is significantly C–X antibonding. The large increase (0.90 eV) of the magnitude of β_{CN} relative to β_{CS} does thus produce a destabilization in the case of the a_2 level. Another factor contributing to the predicted splitting is the circumstance that the magnitude of the α_N value employed is actually somewhat less (0.34 eV) than the magnitude of α_S ; this destabilizes the a_2 level relative to the b_1 level due to the large difference in amplitude on the heteroatoms; see Figures 4 and 8. The results of the MINDO/3 calculations listed in the tables also correspond to a larger destabilization of the a_2 level than of the b_1 level, although the difference is small. We thus tend to assign the ordering of these levels as indicated in Figures 7 and 8 and in Table II.

The fourth and fifth π levels are significantly C–X bonding, and a stabilization of these levels due to the increase of the magnitude of β_{CN} relative to β_{CS} is predicted to dominate over the destabilizing effects. As mentioned above, the predicted stabilization of these levels is expected to be underestimated as in the case of the third π level of pyrrole. The shifts of band ④ in the PE spectra are nevertheless quite accurately predicted by the shifts of the calculated fourth π level; see the tables. We consider it likely that this π level is involved in the ionization process corresponding to band ④, probably overlapping the onset of the σ levels.

The results for the series 4–8–9 can be understood in similar terms as the results for the series 1–7–9. The increase of the magnitude of β_{CN} relative to β_{CS} is very large (1.30 eV) and the increase of the magnitude of α_N relative to α_S is also considerable (0.57 eV). This means that a domination of the stabilizing contributions is predicted already for the third π level; see Figure 8. The observed shifts of this level are not monotonic, however; see Figure 7. Successive replacement of the selenium atoms in 4 by NH groups to yield 8 and 9 shifts band ③ in the PE spectrum first toward lower, then toward higher binding energies, yielding a small overall shift toward higher binding energies. Such a behavior is hinted by the calculated results, and can be explained by a large distortion of the third π orbital in 8 which introduces a C–N antibonding contribution; see Figure 8.

Concluding Remarks

The results of the simple model not only describe a number of qualitative trends, but are also in satisfactory numerical

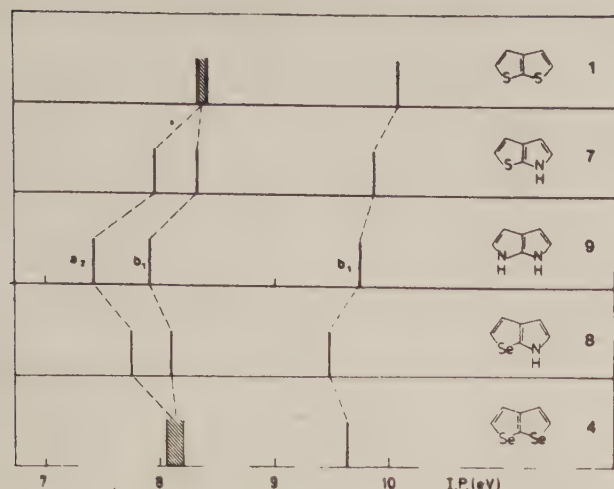


Figure 7. Correlation of the observed first three ionization potentials in the series 1-7-9-8-4; see the tables.

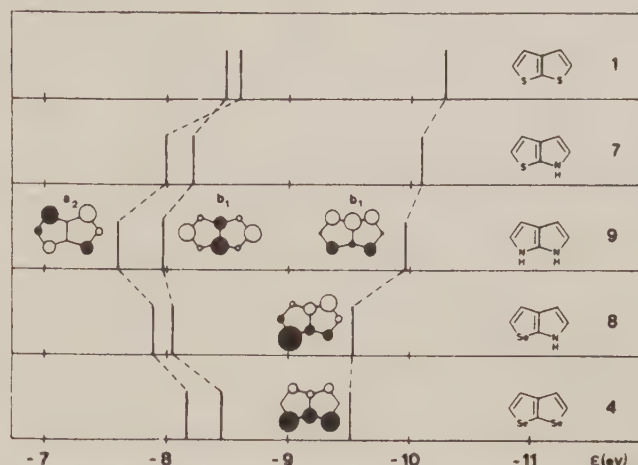


Figure 8. Correlation of the calculated energies of the three highest occupied HMO levels for the series 1-7-9-8-4; see the tables. The shape of the important orbitals is indicated schematically.

agreement with the PE data. This is illustrated by the linear regression of the measured ionization potentials on the calculated orbital energies for all the compounds 1-11; see Figure 9 (the linear regression coefficient is 0.993 and the standard deviation is 0.158 eV). The overall satisfactory performance of the model invites further confidence in the basic concepts behind it.

We may thus conclude that a description of the effects of the heterogroup NH relative to heteroatoms from group VI requires specific attention to the interactions taking place in the σ electron system. In particular, the large polarity of the N-H bond tends to increase the electron density on the ring atoms, implying a large destabilizing inductive effect on the carbon atom frame and a large reduction of the effective electronegativity of the NH group compared with the nitrogen atom. These effects can be described in terms of simple MO theory, which yields a good agreement with the PE data for the series 1-11. It appears that little evidence for these effects can be found from a study of electronic absorption spectra, since the influence on the excited states is similar to the influence on the ground state; this is indicated by the result that calculations with no representation of the effects described above give reasonable excitation energies.³³ We wish furthermore to point out that no direct conclusions regarding the "aromaticity" or "reactivity" of these compounds should be drawn from the present results, since these questions are probably much too complex to be meaningfully discussed in terms of one-electron properties.³⁴

III. Experimental Section

The compounds 3-11 were prepared according to the prescriptions in the literature.⁸⁻¹³

The PE spectra were recorded on a PS 18 photoelectron spectrometer (Perkin-Elmer Ltd., Beaconsfield) equipped with a heated probe. In the case of 9 the sample was heated to 105 °C; in the remaining cases the temperature was close to 30 °C. The spectra were calibrated with argon, and a resolution of about 20 meV on the argon line was obtained. Each spectrum was recorded several times to ensure the reproducibility of the results.

Calculations. The HMO⁵ calculations were carried out on a Hewlett-Packard 9800-30 computer. The parameters applied are discussed in detail in the paper. The EWMO,^{17,18} CNDO/2,¹⁹ and MINDO/3²⁰ calculations were performed on the IBM 370/168 computer at the computing center of the TH Darmstadt, using double precision versions of computer programs published by QCPE, Indiana University. The standard parameters inherent in the programs were employed.¹⁸⁻²⁰

For the calculations on furan, pyrrole, and thiophene the geometries determined by microwave spectroscopy²⁵ were employed. In case of the compounds 1-11 the geometries were estimated from the exper-

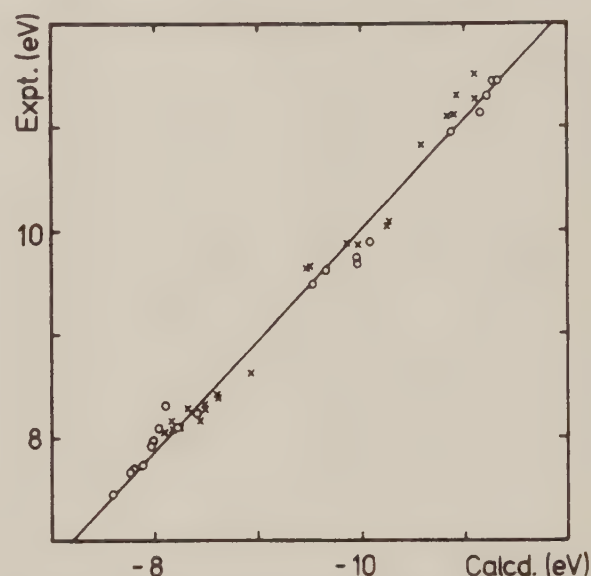


Figure 9. Linear regression of the experimental ionization potentials on the calculated HMO orbital energies for the compounds 1-11; see the tables. The crosses correspond to the compounds 1-6, and circles correspond to the NH containing species 7-11.

imental geometries of thiophene,²⁵ selenophene,³⁵ and pyrrole²⁵ by simple fusion of the constituent rings. For the "mixed" compounds 3, 5, 7, 8, 10, and 11 the length of the central C-C bond was taken as 1.37 Å.

Acknowledgment. We are grateful to the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support.

Registry No.—Furan, 110-00-9; pyrrole, 109-97-7; thiophene, 110-02-1; selenophene, 288-05-1.

References and Notes

- (1) Part 24 of "Electronic Structure of Sulfur Compounds". Part 23: R. Bartetzko and R. Gleiter, *J. Chem. Soc., Chem. Commun.*, in press.
- (2) Darmstadt.
- (3) Lund.
- (4) Dijon.
- (5) (a) M. J. S. Dewar and R. C. Dougherty, "The PMO Theory of Organic Chemistry", Plenum Press, New York, N.Y., 1975; (b) E. Heilbronner and H. Bock, "Das HMO Modell und seine Anwendung", Verlag Chemie, Weinheim/Bergstr., Germany, 1968; (c) A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists", Wiley, New York, N.Y., 1961.
- (6) J. H. D. Eland, *J. Mass Spectrom. Ion Phys.*, **2**, 471 (1969).
- (7) W. Schäfer, A. Schweig, S. Gronowitz, A. Taticchi, and F. Fringuelli, *J. Chem. Soc., Chem. Commun.*, 541 (1973).
- (8) A. Bugge, *Acta Chem. Scand.*, **23**, 1823 (1969).
- (9) S. Gronowitz and A. Konar, to be published.

- (10) A. Bugge, *Acta Chem. Scand.*, **24**, 1953 (1970).
- (11) S. Gronowitz, T. Frejd, and A.-B. Hörnfeldt, *Chem. Scr.*, **5**, 236 (1974).
- (12) S. Soth, M. Farnier, and P. Fournari, *Bull. Soc. Chim. Fr.*, 2511 (1975).
- (13) K. N. Java, S. Soth, M. Farnier, and C. Paulmier, *C. R. Acad. Sci.*, **281**, 793 (1975).
- (14) P. A. Clark, R. Gleiter, and E. Heilbronner, *Tetrahedron*, **29**, 3085 (1973).
- (15) L. Pauling, "The Nature of the Chemical Bond", 3rd ed, Cornell University Press, Ithaca, N.Y., 1960.
- (16) T. Koopmans, *Physica*, **1**, 104 (1934).
- (17) J. Linderberg and Y. Örn, "Propagators in Quantum Chemistry", Academic Press, New York, N.Y., 1973.
- (18) J. Spanget-Larsen, *J. Electron Spectrosc. Relat. Phenom.*, **2**, 33 (1973); **3**, 369 (1974). Computer Program MIEHM, QCPE 246, Indiana University, 1974.
- (19) J. A. Pople and D. L. Beveridge, "Approximate Molecular Orbital Theory", McGraw-Hill, New York, N.Y., 1970.
- (20) R. C. Bingham, M. J. S. Dewar, and D. H. Lo, *J. Am. Chem. Soc.*, **97**, 1285 (1975), and subsequent papers.
- (21) R. Gleiter, M. Kobayashi, J. Spanget-Larsen, J. P. Ferraris, A. N. Bloch, K. Bechgaard, and D. O. Cowan, *Ber. Bunsenges. Phys. Chem.*, **79**, 1218 (1975).
- (22) W. von Niessen, W. P. Kraemer, and L. S. Cederbaum, *J. Electron Spectrosc. Relat. Phenom.*, **8**, 179 (1976).
- (23) E. Clementi, H. Clementi, and D. R. Davis, *J. Chem. Phys.*, **46**, 4725 (1967).
- (24) See any introductory textbook on quantum chemistry.
- (25) L. Nygaard, J. T. Nielsen, J. Kirchheimer, G. Maltesen, J. Rastrup-Andersen, and G. O. Sørensen, *J. Mol. Struct.*, **3**, 491 (1969), and references cited therein.
- (26) (a) G. Distefano, S. Pignataro, G. Innorta, F. Fringuelli, G. Marino, and A. Taticchi, *Chem. Phys. Lett.*, **22**, 132 (1973); (b) F. Fringuelli, G. Marino, A. Taticchi, G. Distefano, F. P. Colonna, and S. Pignataro, *J. Chem. Soc., Perkin Trans. 2*, 276 (1976).
- (27) W. von Niessen, L. S. Cederbaum, and G. H. F. Dierksen, *J. Am. Chem. Soc.*, **98**, 2066 (1976).
- (28) A. D. Baker, D. Betteridge, N. R. Kemp, and R. E. Kirby, *Anal. Chem.*, **42**, 1064 (1970).
- (29) A similar explanation has been given for the observed lowering of the first ionization potential in the series of 1,6,6a-trithiapentalene and its aza analogues; see R. Gleiter, R. Gygax, and D. H. Reid, *Helv. Chim. Acta*, **58**, 1591 (1975).
- (30) This result is in disagreement with the expectation expressed by N. D. Epiotis, W. R. Cherry, F. Barnardi, and W. J. Hehre, *J. Am. Chem. Soc.*, **98**, 4361 (1976).
- (31) $\alpha_{\text{C}}^{\text{adj}}$ refers to a position adjacent to an NH group. The effect of two neighboring NH groups is taken as twice the effect of one, e.g., in the case of **9**.
- (32) The HMO results for pyrrolo[3,2-*b*]pyrrole are $3a_u(\pi)$, -7.51 eV; $2a_u(\pi)$, -8.20 eV; $2b_g(\pi)$, -9.65 eV; $1b_g(\pi)$, -11.59 eV. This compound was not available for the measurements.
- (33) J. Fabian, A. Mehlhorn, and R. Zahradnik, *Theor. Chim. Acta*, **12**, 247 (1968).
- (34) G. Marino, *Adv. Heterocycl. Chem.*, **13**, 235 (1971).
- (35) R. D. Brown, F. R. Burden, and P. D. Godfrey, *J. Mol. Spectrosc.*, **25**, 415 (1968).

Paper E

Selenolo [3,4-b] thiophene - An Attempted Synthesis of the Fourth
"Classical" Selenolothiophene.

Selenolo[3,4-b]thiophene - an Attempted Synthesis of the Fourth
"Classical" Selenolothiophene

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Lund, Sweden

Abstract

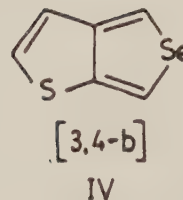
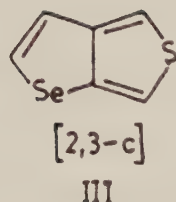
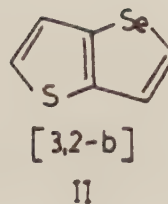
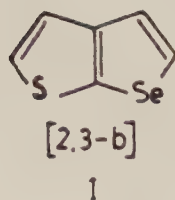
Selenolo[3,4-b]thiophene - an attempted synthesis of the fourth "classical" selenolothiophene. Konar, A.; Gronowitz, S. (Division of Organic Chemistry 1, Chemical Center, University of Lund, P.O. Box 740, S-220 07 Lund, Sweden).

Chemica Scripta (Sweden)

The synthesis of 2-carbomethoxyselenolo[3,4-b]thiophene, a derivative of the last, hitherto unknown "classical" selenolothiophene, is described. The attempted hydrolysis of the ester function yields the dimeric acid X along with some other polymeric products, and not the expected 2-carboxyselenolo[3,4-b]thiophene, the decarboxylation of which would give the parent selenolo[3,4-b]thiophene.

Introduction

Heteroaromatic systems containing fused thiophene and selenophene rings were unknown until recently. If one not takes into account the "non-classical" structures, with the formally tetravalent sulfur or selenium atom, there are four possible ways to annelate one thiophene and one selenophene ring, which give the four selenolothiophenes I-IV, as shown below:



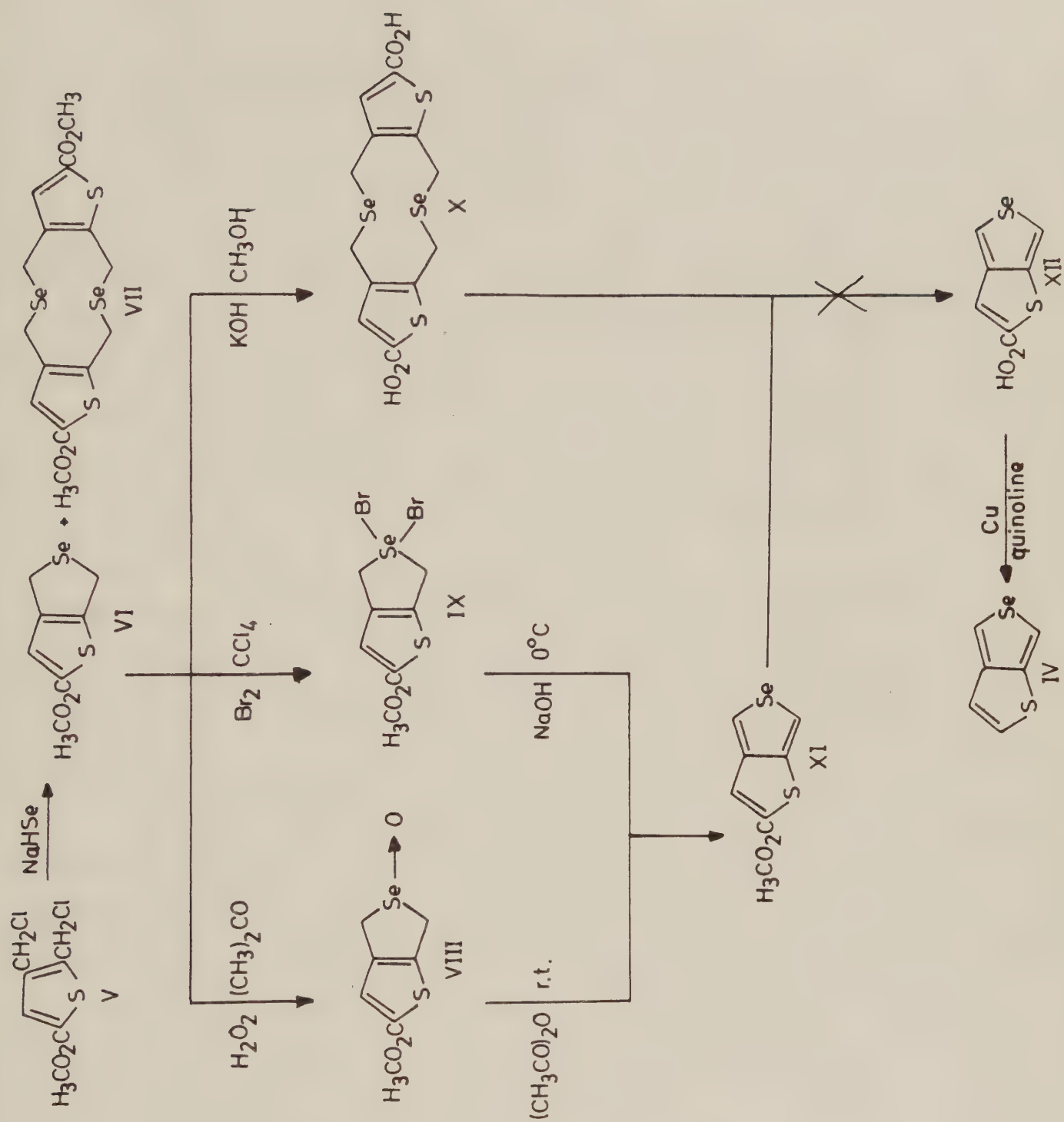
A review by Litvinov and Goldfarb [1] covering work on thienothiophenes and related systems published until the first half of 1974 had appeared. In the review, also selenoloselenophenes were briefly discussed. In 1973, Litvinov et al. [2] also published a review dealing exclusively with selenolothiophenes, where their syntheses and some physical properties were summarized. To the best of our knowledge, since that time, only a few reports concerning selenolothiophenes have appeared.

NBS-bromination and Vilsmeier formylation of I and II [3], and metalation of I [4] were studied by Litvinov et al., whereas we studied the photoelectron spectra of I and II [5], electrophilic substitution reactions of II [6] and Vilsmeier formylation and metalation of III [7].

An attempted synthesis of the fourth possible isomer IV is the subject of the present paper.

Results and Discussion

Ring-closure of the ortho-bifunctional thiophene derivatives is one of the most convenient and widely used methods for the synthesis of thieno- or selenolothiophenes. Both I [8] and II [9] were prepared by Dieckmann cyclizations of the appropriate formyl thienylselenoacetates, but this approach was unsuccessful for the synthesis of III [10], as well as for its selenium analogue, selenolo[3,4-b]-selenophene [11]. Our attempt to prepare IV in a similar manner also proved unsuccessful - only resinification products were obtained in the reaction of n-butyllithium with 2-(4-bromo-3-selenienyl)-1,3-dioxolane and subsequent treatment of the product with sulfur and methylbromoacetate. Both III [10] and selenolo[3,4-b]-selenophene [11] were instead synthesized via quaternization of 4-methylseleno-3-thiophene and -selenophene aldehyde, respectively, and ring-closure of the intermediate selenonium salts with pyridine and acetic anhydride. We have not tried the corresponding approach to IV, which would proceed through a quaternary sulfonium salt, but adopted the synthetic route of Wynberg et al. [12,13], who prepared thieno[3,4-b]thiophene by dehydration of dihydrothienothiophene sulfoxide. Similar dehydration of dihydroselenophene selenoxides, as well as dehydrobromination of selenium dibromides, was previously used by us [14] in preparing the "non-classical" [3,4-c]-annelated selenolo-selenophenes, and both of these reactions were employed in our present attempts to prepare IV along the route outlined in Scheme I.



Scheme I

We have carried out a similar reaction sequence starting with the selenium analogue of V, and succeeded in preparing selenolo[3,4-b]-selenophene, although in very low yield [11]. In both cases, the critical step is the cyclization of the bischloromethylselenophene or -thiophene with sodium hydrogen selenide, which gives predominantly the dimeric and higher oligomeric products. We have carried out the cyclization of V at various temperatures, in such solvents as ethanol, dioxane and water, varying the order of addition of reagents and also using a high-dilution technique, but the yield of the desired dihydroselenolothiophene VI never exceeded 15 %. In contrast, a similar cyclization of V with sodium sulfide in methanol, which was carried out by Wynberg *et al.* [13], gave the monomeric dihydrothienothiophene in 66 % yield. Subsequent hydrolysis of the ester function afforded the expected acid in 92 % yield. However, all our attempts to hydrolyze VI in a similar manner ended up with the dimeric acid X [15], which also was the case with the selenium analogue of VI [11].

For this reason, we left the ester group of VI intact until the aromatic nucleus of selenolo[3,4-b]thiophene was formed, an approach which had worked in the case of selenolo[3,4-b]selenophene [11]. Oxidation of VI with hydrogen peroxide in acetone afforded the selenoxide VIII, and bromination with bromine in carbon tetrachloride gave the selenium dibromide IX in good yields. Both VIII and IX could be transformed to 2-carbomethoxyselenolo[3,4-b]thiophene XI, hydrolysis and decarboxylation of which would give the parent selenolo[3,4-b]thiophene (IV). Formation of the aromatic system in XI from the selenoxide VIII occurred spontaneously on warming, and could be conveniently observed by NMR. The transition was, however, only

partial according to NMR, and the complete reaction was achieved preparatively by adding acetic anhydride at 0°C, since the reaction is exothermic and can lead to the decomposition of XI. It is noteworthy that the transformation of the selenium dibromide IX into XI could be carried out by concentrated sodium hydroxide solution without hydrolysis of the ester function. In the dehydration of the selenoxide VIII with acetic anhydride, selenide VI was formed in small amounts, in addition to the aromatic system XI. Unfortunately, the intended hydrolysis of XI to 2-carboxyselenolo[3,4-b]thiophene (XII) turned out to be the most critical step in the reaction sequence. Although the ester group of XI was actually hydrolyzed, the destruction of the selenophene ring occurred at the same time, giving rise to the dimeric acid X [15], along with a lot of resinification products.

Thus, the proposed synthetic approach to the fourth selenolothiophene IV as outlined in Scheme I proved impracticable. As already mentioned, the most commonly used approach to selenolothiophenes, i.e. in this case the cyclization of 2-(4-bromo-3-selenienyl)-1,3-dioxolane, was also unsuccessful. Other possible routes to IV might be the way analogous to the preparations of III [10] and selenolo[3,4-b]selenophene [11] via quaternization of 4-methylthio-3-selenophene aldehyde with methyl bromoacetate or via the route described by Mac Dowell and Patrick [16] for the preparation of 4,6-dihydrothieno[3,4-b]thiophene. The first approach to IV would, however, suffer from the necessity of passing through the ester XI, the hydrolysis of which might cause the above-mentioned difficulties. The other route, though very laborious, would lead directly to the unsubstituted system without involving hydrolysis and decarboxylation. It requires 2,3-bisbromomethylthiophene as starting material, which was prepared by Mac Dowell and Patrick [16] in five steps from 3-thiophene aldehyde in 35 % yield. Its cyclization with sodium hydrogen

selenide followed by oxidation and dehydration of the selenoxide formed might then afford the desired parent compound IV. The main drawback of this approach would probably be the difficulties encountered earlier in the cyclization step, although it is difficult to predict how the absence of an electron-withdrawing substituent in the thiophene ring would influence the reaction course. On the other hand, the 2-carbomethoxy substituent has certainly a stabilizing effect on the selenolothiophene system in XI, and the necessity of working with the unsubstituted 4,6-dihydroselenolo[3,4-b]thiophene, which we expect to be unstable, might prove another serious drawback of the reaction sequence proposed. The instability of 4,6-dihydrothienothiophene is known [16], and our results concerning selenolo[3,4-b]thiophene (IV) also indicate its instability compared with the [2,3-c]-annelated analogue (III).

In our opinion, the most feasible way to IV would, after all, be the route of Scheme I, modified in the hydrolysis step of XI, which should be achieved under neutral or slightly acidic conditions. A reagent which has gained use in the cleavage of esters is iodotrimethylsilane, and a convenient alternative to it in form of a mixture of chlorotrimethylsilane and sodium iodide in acetonitrile has recently been reported by Olah et al. [17]. We intend to use this method in our future attempts to prepare selenolo[3,4-b]thiophene (IV), which still is the ultimate goal of our work.

Experimental

The ^1H NMR spectra were recorded on a JEOL MH 100 high resolution spectrometer. Mass spectra were recorded on a Finnigan Model 4021 mass spectrometer, and analytical GLC was carried out with a Perkin-Elmer 900 gas chromatograph connected to a Varian 480 digital integrator. The integrator was not calibrated. A Dexil 300 3 % on Chromosorb W AW column was used for all gas chromatographic analyses. The IR spectra were recorded on a Perkin-Elmer 900 instrument. Elementary analyses were carried out by Ilse Beetz, Mikroanalytisches Laboratorium, Kronach, Germany.

2-Carbomethoxy-4H,6H-dihydroselenolo [3,4-b] thiophene (VI).

To a colourless solution of 0.11 mol of sodium hydrogen selenide in 1.5 l of abs. ethanol prepared according to Ref. 18, 23.9 g (0.1 mol) of solid bischloromethyl compound V was added in small portions during 5 hours with stirring at room temperature under a nitrogen atmosphere. After complete addition, the reaction mixture was stirred overnight at room temperature and the precipitated sodium chloride was filtered off. The slightly yellow filtrate was concentrated to about 300 ml and poured into 1 l of water. The resulting white suspension was extracted with chloroform, and the combined extracts were dried over magnesium sulfate and concentrated, leaving 15.3 g (62 %) of a mixture of the desired product VI and its dimer VII. Separation of the monomer was achieved by fractional crystallization from aqueous ethanol, and gave 3.7 g (15 %) of the title compound as light yellow needles, m.p. 97-99°C. NMR (CDCl_3): δ 3.86 (s, 3H, $-\text{CO}_2\text{CH}_3$),

7.43 (s, 1H, H₃), and a strongly coupled AA'BB' spectrum of the methylene protons centred at 4.06 and 4.20. If the spectrum was recorded in a DMSO-d₆ solution, the multiplets of the methylene protons collapsed to sharp singlets at δ 4.97 and 5.27. NMR (DMSO-d₆): δ 3.96 (s, 3H, -CO₂CH₃), 4.97 (s, 2H, CH₂), 5.27 (s, 2H, CH₂), 8.01 (s, 1H, H₃). Anal. Calcd. for C₈H₈O₂SSe: C 38.87; H 3.26; Se 31.94. Found: C 39.02; H 3.36; Se 31.79.

2,8-Biscarbomethoxy-4H,6H,10H,12H-dithieno[3,2-c:2',3'-h][1,6]-diselenecin (VII), (see note 15), (9.9 g, 40 %), m.p. 208-210°C, was obtained after recrystallization from pyridine/water (9:1). Owing to its low solubility in organic solvents, no NMR spectrum could be recorded. Anal. Calcd. for C₁₆H₁₆O₄S₂Se₂: C 38.87; H 3.26; Se 31.94. Found: C 38.71; H 3.38; Se 32.08.

2-Carbomethoxy-4H,6H-dihydroselenolo[3,4-b]thiophene 5-oxide (VIII).

To a solution of 3.7 g (15.0 mmol) of the selenide VI in 20 ml of dry tetrahydrofuran, cooled to -10°C in an ice-salt bath, a solution of 1.9 g (16.8 mmol) of 30 % hydrogen peroxide in 10 ml of dry tetrahydrofuran was added dropwise with stirring. The reaction was monitored by TLC (silica gel plates with ethyl acetate/petroleum ether, b.p. 40-60°C, 1:4 developer). After 15 min, a precipitate was formed, but the starting material was still observed on TLC even after 1 hour, and thus an additional 0.5 g of hydrogen peroxide solution was added. Two more 0.3 g portions of hydrogen peroxide were required to bring the reaction to completion, whereupon the reaction mixture was concentrated in vacuo and filtered to give 3.0 g (76 %) of the selenoxide VIII, m.p. 76-78°C with decomposition. All attempts at purification resulted in decomposition. Anal. Calcd. for C₈H₈O₃SSe:

C 36.51; H 3.06; Se 30.03. Found: C 36.35; H 3.09; Se 30.03.

Due to the low solubility of the selenoxide in CDCl_3 , CDBr_3 and C_6D_6 , the NMR spectrum could only be recorded in DMSO-d_6 solution. If the spectrum was recorded immediately after dissolving the compound, the expected signals of the methylene protons appeared as two singlets at δ 3.85 and 3.88, together with a singlet for the ester group at δ 3.81 and a singlet for the aromatic proton in the 3-position of the thiophene ring at δ 7.62. If, however, the spectrum was recorded after a short period of time or after slight warming of the DMSO -solution, the intensity of the methylene protons diminished and the aromatic part of the spectrum indicated formation of the selenolo[3,4-b]thiophene system. Thus, the two α -protons of the selenophene ring appeared at δ 8.71 (d, 1H, H_4) and δ 8.32 (2xd, 1H, H_6) with the coupling constant $J_{\text{H4-H6}} = 2.3$ Hz and a long-range coupling to the β -proton of the thiophene ring, $J_{\text{H3-H6}} = 0.75$ Hz. This proton gave a signal at δ 7.68 (d, 1H, H_3).

2-Carbomethoxy-4H,6H-dihydroselenolo[3,4-b]thiophene

5,5-dibromide (IX). To a cooled solution of 0.50 g (2.0 mmol) of the selenide VI in 5 ml of methylene chloride, a solution of 0.35 g (2.2 mmol) of bromine in 5 ml of methylene chloride was added dropwise with stirring. On standing, fine yellow crystals slowly precipitated, several drops of cyclohexane were added to aid in the precipitation. Filtration gave 0.49 g (60 %) of the selenium dibromide IX, m.p. $114\text{--}118^\circ\text{C}$, with decomposition. All attempts at purification resulted in decomposition. No satisfactory elementary analysis could be obtained. NMR (CDCl_3): δ 3.88 (s, 3H, $-\text{CO}_2\text{CH}_3$), 4.48 (s, 2H, CH_2), 4.69 (s, 2H, CH_2), 7.70 (s, 1H, H_3).

2,8-Dicarboxy-4H,6H,10H,12H-dithieno[3,2-c:2',3'-h] [1,6] diselenecin (X)

The selenide VI (0.50 g, 2.0 mmol) was added to a solution of 0.28 g (5.0 mmol) of potassium hydroxide in 50 ml of methanol, and the resulting solution was refluxed for 1 hour, and then poured into 200 ml of water. The dark mixture was filtered, cooled and acidified with cold 2N hydrochloric acid, leaving 0.21 g (45 %) of the acid X [15], m.p. 240-244°C. Owing to its low solubility in organic solvents, no NMR spectrum could be recorded. In the mass spectrum, the peaks centred at m/e 468 (M^+ , 12 %) showed the same pattern as a spectrum simulated for two selenium and two sulfur atoms, whereas the peaks centred at m/e 234 (base peak) for one selenium and one sulfur atom selenium-sulfur.

Anal. Calcd. for $C_{14}H_{12}O_4S_2Se_2$: C 36.06; H 2.59; Se 33.87.

Found: C 36.27; H 2.41; Se 34.23.

2-Carbomethoxyselenolo[3,4-b]thiophene (XI) from the selenoxide VIII. The selenoxide VI (0.53 g, 2.0 mmol) was dissolved in 10 ml of acetic anhydride at 0°C, whereupon a spontaneous exothermic reaction took place and the solution became red and then very dark. After stirring at room temperature for 0.5 h, excess acetic anhydride was hydrolyzed with water, the reaction mixture was extracted with ether, and the ether extracts were washed with saturated sodium hydrogen carbonate solution and water, dried over magnesium sulfate and concentrated. Attempts to purify the dark, oily residue, by crystallization from methanol, led to partial decomposition, as shown by the precipitation of black, elemental selenium. In the next runs, the crude reaction product was instead subjected to flash chromatography according to Ref. 19, using a mixture of ethyl acetate and petroleum ether, b.p. 40-60°C, in a ratio 1:4 as eluent. This gave 0.05 g (10 %)

of selenide VI and 0.22 g (44 %) of 2-carbomethoxyselenolo[3,4-b]-thiophene (XI), m.p. 78-80°C. All attempts at further purification led to decomposition. NMR (CDCl₃): δ 3.82 (s, 3H, -CO₂CH₃), 7.43 (d, 1H, H₃), 7.78 (2Xd, 1H, H₆), 8.18 (d, 1H, H₄). $J_{\text{H4-H6}} = 2.4$ Hz, $J_{\text{H3-H6}} = 0.8$ Hz. Anal: Calcd. for C₈H₆O₂SSe: C 39.19; H 2.47; Se 32.21. Found: C 39.91; H 2.36; Se 33.11.

2-Carbomethoxyselenolo[3,4-b]thiophene (XI) from the selenium dibromide IX. The selenium dibromide IX (0.41 g, 1.0 mmol) was added to 20 ml of cold 20 % sodium hydroxide solution and stirred for 20 min at 0°C. Hexane (10 ml) was then added, and during the next 10 min of stirring, the upper hexane layer became orange, as selenolothiophene XI was liberated into the organic phase. The reaction mixture was then extracted with ether, washed with water until neutral pH, dried over magnesium sulfate and concentrated. Purification of the oily residue, by flash chromatography under the conditions given above, afforded 0.16 g (65 %) of XI, with m.p. and NMR spectrum in accord with those for 2-carboxyselenolo[3,4-b]thiophene obtained by dehydration of the selenoxide VIII.

Attempts to hydrolyze 2-carbomethoxyselenolo[3,4-b]thiophene (XI) to the acid XII. Compound XI (0.22 g, 0.09 mmol) was added to a solution of 0.11 g (2.0 mmol) of potassium hydroxide in 20 ml of methanol and the resulting dark mixture was stirred at room temperature for 0.5 h. It was then filtered from the black precipitate, diluted with water, cooled and acidified with 1N hydrochloric acid, leaving 0.09 g (43 %) of the acid X, with m.p. and mass spectrum in accord with those given above. Regarding the structure of X, see note 15.

Similar results were obtained if an aqueous solution of potassium hydroxide was used.

Acknowledgement

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References

1. Litvinov, V.P. and Goldfarb, Ya.L., Advan. Heterocycl. Chem. 1976, 19, 123.
2. Litvinov, V.P., Goldfarb, Ya.L., Bogdanov, V.S., Konjaeva, I.P. and Sukiasyan, A.N., J. prakt. Chem. 1973, 315, 850.
3. Litvinov, V.P., Goldfarb, Ya.L. and Konjaeva, I.P., Izvest. Akad. Nauk SSSR, Ser. Khim. 1979, 372.
4. Litvinov, V.P., Konjaeva, I.P. and Goldfarb, Ya.L., Izvest. Akad. Nauk SSSR, Ser. Khim. 1976, 477.
5. Gleiter, R., Kobayashi, M., Spanget-Larsen, J., Gronowitz, S., Konar, A. and Farnier, M., J. Org. Chem. 1977, 42, 2230.
6. Gronowitz, S., Konar, A. and Litvinov, V.P., Chemica Scripta, in press.
7. Gronowitz, S., Konar, A. and Litvinov, V.P., Izvest. Akad. Nauk SSSR, Ser. Khim, in press.
8. Bugge, A., Acta Chem. Scand. 1969, 23, 1823.
9. Goldfarb, Ya.L., Litvinov, V.P. and Ozolin, S.A., Izvest. Akad. Nauk SSSR, Ser. Khim. 1968, 1419.
10. Litvinov, V.P., Sukiasyan, A.N., Goldfarb, Ya.L. and Bogacheva, L.V., Izvest. Akad. Nauk SSSR, Ser. Khim. 1971, 1592.
11. Konar, A. and Gronowitz, S., Tetrahedron, in press.
12. Wynberg, H. and Zwanenburg, D.J., Tetrahedron Lett. 1967, 761.
13. Zwanenburg, D.J., de Haan, H. and Wynberg, H., J. Org. Chem. 1966, 31, 3363.
14. Gronowitz, S. and Konar, A., J. Chem. Soc., Chem. Commun. 1977,

15. For the sake of simplicity only one of the two possible structures of VII and X have been drawn in Scheme I and are referred to in the Experimental Part. Although TLC and sharp melting points of VII and X indicate the presence of only one isomer of both compounds, we do not know if the isomers with "cis" or "trans" arrangement of the thiophene rings had formed.
16. Mac Dowell, D.W.H. and Patrick, T.B., J. Org. Chem. 1966, 31, 3592.
17. Olah, G.A., Narang, S.C., Gupta, B.G.B. and Malhotra, R., J. Org. Chem. 1979, 44, 1247.
18. Klayman, D.L. and Griffin, T.S., J. Am. Chem. Soc. 1973, 95, 197.
19. Still, W.C., Kahn, M. and Mitra, A., J. Org. Chem. 1978, 43, 2923.

Paper F

Selenolo [3,4-b] selenophene - the Third "Classical" Selenophene.

Paper F

Selenolo [3,4-b] selenophene - the Third "Classical" Selenophene.

SELENOLO[3,4-b]SELENOPHENE - THE THIRD "CLASSICAL" SELENOPHTENE

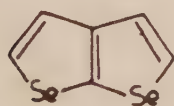
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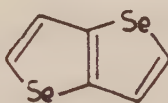
Abstract

Selenolo[3,4-b]selenophene (3) has been synthesized by two different routes using 2,3-bischloromethyl-5-carbomethoxyselenophene (4) or preferably 4-methylseleno-3-selenophene aldehyde (10) as the starting material. In marked contrast to its thiophene analogue thieno[3,4-b]thiophene, 3 was stable. Analysis of the ^1H , ^{13}C and, in particular, the ^{77}Se NMR gave strong evidence for the more positive nature of the Se-5 than the Se-1 atom of 3.

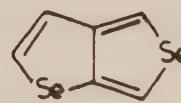
Previously¹ we have described the syntheses of selenolo[2,3-b]selenophene (1) and selenolo[3,2-b]selenophene (2) from the suitable selenienyl-1,3-dioxolanes via a ring-closure of the intermediate formyl selenienyl-selenoacetates with sodium ethoxide.



1



2



3

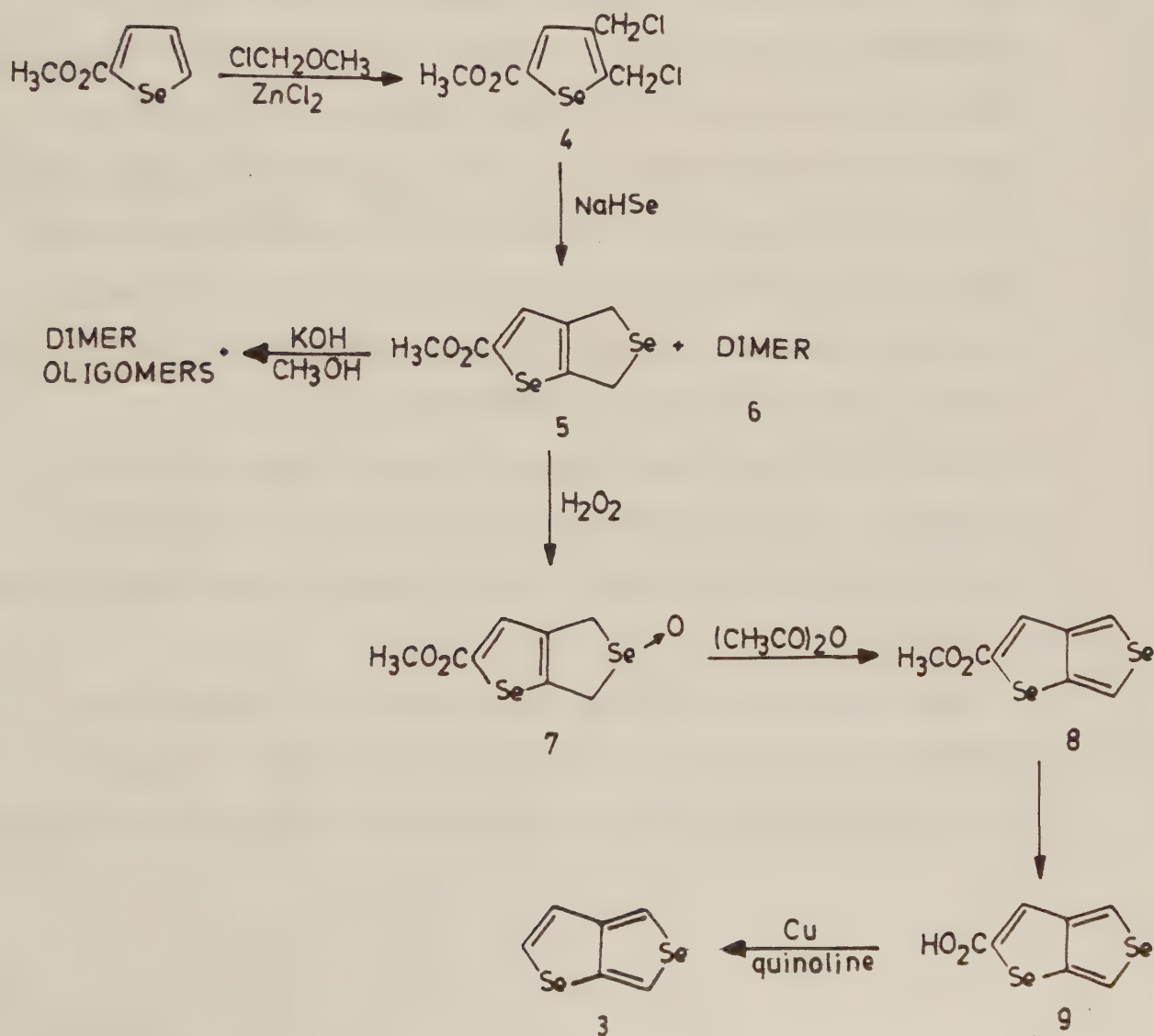
We now wish to report the synthesis of selenolo[3,4-b]selenophene (3), the third selenophtene with a "classical" structure. The isomeric selenophtenes 1-3 were claimed by Umezawa² to be present among the products of the reaction between acetylene and selenium. However, we were not able to provide evidence for the presence of any other selenophtene than selenolo[3,2-b]selenophene (2) among the more than 30 identified products of this reaction. Moreover, Umezawa's structural

assignments were shown by us^{1,3} to be erroneous and the synthesis of the third selenophthene 3 would be the final piece of evidence for the structures. There are few described synthetic routes leading to the sulfur analogues of selenophthenes 1-3. The most common ones utilize a ring-closure of a suitably substituted thiophene leading directly to a derivative of the aromatic, fused system. Analogously, our syntheses of 1 and 2 were accomplished by Dieckmann cyclizations of the above-mentioned formyl selenienylselenoacetates. This synthetic approach was also successful for the preparation of 2-carboxythieno[3,4-b]thiophene,⁴ (i.e. ring-closure on the 3- and 4-positions of the thiophene ring), but failed when applied to the synthesis of selenolo[2,3-c]thiophene.⁵ Also, our attempt to prepare selenolo[3,4-b]selenophene (3) in a similar manner proved unsuccessful - only resinification products were obtained in the reaction of n-butyllithium with 2-(4-bromo-3-selenienyl)-1,3-dioxolane and subsequent treatment of the product with red selenium and methyl bromoacetate.

Other possible approaches might be a method of Wynberg and Zwanenburg,⁶ who utilized a dehydration of a dihydrothienothiophene sulfoxide for a synthesis of thieno[3,4-b]thiophene, and the path of Litvinov et al.,⁵ who synthesized selenolo[2,3-c]thiophene via quaternization of 4-methylseleno-3-thiophene aldehyde and ring-closure of the intermediate selenonium salt in pyridine and acetic anhydride.

Initially, we tried the approach of Wynberg and Zwanenburg,⁶ partly because of our previous experience in preparing the "non-classical" [3,4-c]annelated selenoloselenophenes (similarly via dehydration of dihydro-

selenoloseienophene selenoxides or the dehydrobromination of selenium dibromides⁷⁾ and partly because, by starting from a thiophene derivative, this route could also lead to the fourth possible "classical" selenolothiophene, namely the currently unknown selenolo-[3,4-b]thiophene. Work on its synthesis is now in progress in our laboratory. The synthesis of 3 along the route mentioned is outlined in Scheme 1.

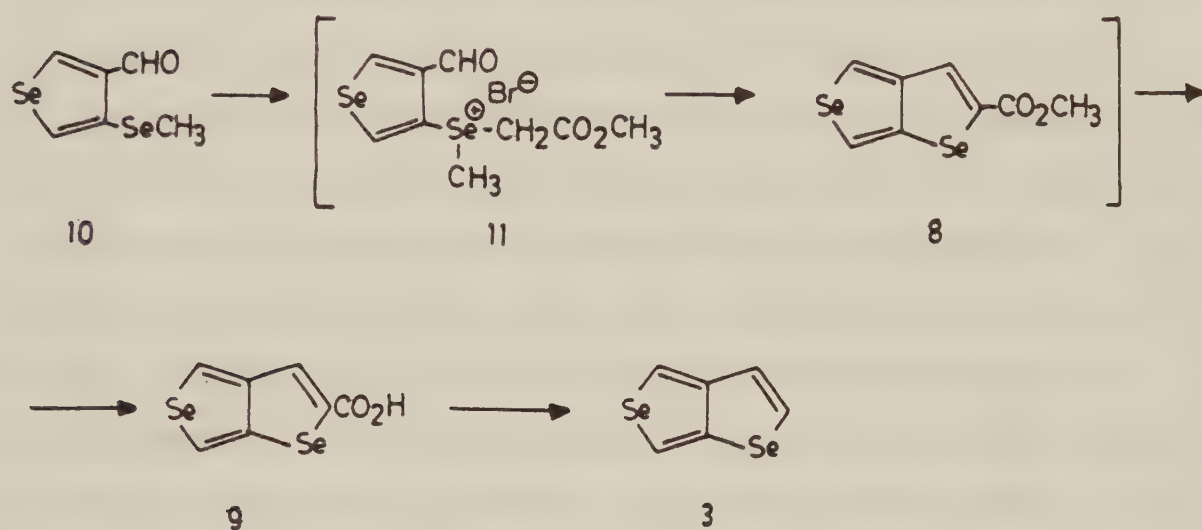


Scheme 1

This sequence is similar to that described by Wynberg et al.⁸ for the synthesis of 2-carboxy-4,6-dihydrothieno[3,4-b]thiophene-5-oxide, with the exception that the hydrolysis of the ester function to an acid was done firstly on the aromatic system 8 and not on the dihydroselenophene derivative 5. The reason for this was that the hydrolysis of 5, even under very mild basic conditions, led to the corresponding acid in very low yields - the dimer, trimer and even higher oligomers, as identified by mass spectroscopy, being the main products. This fact indicates the ease with which the dihydroselenophene ring in 5 undergoes (a base-induced) ring-opening, which might also account for the very low yield (< 15 %) of 5 in the cyclization reaction. This reaction gives primarily the dimeric product 6 in varying yields, depending on the conditions employed. We have carried out the cyclization of 4 at various temperatures, using a high dilution technique and varying the order of addition of the reagents, in such solvents as ethanol, water and dioxane but the yield of the desired monomeric product 5 never exceeded 15 %. In contrast, a similar cyclization of a thiophene analogue of 4 with sodium sulfide in methanol gave the required dihydrothienothiophene in 66 % yield.⁸

Nevertheless, the reaction sequence outlined in Scheme 1 was accomplished, the over-all yield of the selenophene 3 being 2.6 % from the bischloromethyl derivative 4 or 1.3 % based on selenophene.

Because of the low, over-all yield in this multi-step synthesis, the approach of Litvinov et al.⁵ was tried, giving selenolo[3,4-b]-selenophene (3) in 44 % yield when starting from the aldehyde 10 or in 18 % from selenophene. The synthetic path is outlined in Scheme 2.



Scheme 2

4-Methylseleno-3-selenophene aldehyde 10 was obtained in 55 % yield in two steps from 3,4-dibromoselenophene by halogen-metal exchange with n-butyllithium and reaction with dimethyl diselenide followed by another lithiation and formylation with N,N-dimethyl formamide. It was also obtained, though in lower yield, via 4-bromo-3-selenophene aldehyde by protecting the aldehyde function as an acetal, reacting with n-butyllithium and dimethyl diselenide and then hydrolyzing the acetal group. This route was more laborious not only because of the greater number of steps but also because the lithiation and subsequent formylation of 3,4-dibromoselenophene always gave a difficult-to-separate mixture of 4-bromo-3-selenophene aldehyde and the starting material, as previously pointed out by Paulmier et al.⁹ The separation was best achieved after acetalization, from which the unreacted 3,4-dibromoselenophene could be recovered by distillation.¹⁰ The methylseleno group of the aldehyde 10, obtained in either way, was quaternized with methyl bromoacetate in toluene to give an intermediate selenonium salt 11, which was then cyclized with acetic anhydride and pyridine to give the ester 8. This was then, without isolation, hydrolyzed to the acid 9, the whole sequence thus being a one-pot reaction from 10, giving 2-carboxyselenolo[3,4-b]selenophene (9) in 61 % yield. Decarboxylation with copper in quinoline gave selenolo[3,4-b]selenophene (3) as light yellow, glistening, volatile crystals, m.p. 46-47°C, in 72 % yield. The compound appeared to be indefinitely stable when kept in a refrigerator and at least for a week at room temperature in air, after which it began to darken. It was also stable in n-pentane solution.

This behaviour is in marked contrast to the behaviour of its sulfur analogue, thieno[3,4-b]thiophene, which rapidly turned yellow on standing in air and was only stable, for a few days, in petroleum ether solution or when kept at -40°C .⁶

The greater stability of **3** compared with thieno[3,4-b]thiophene, together with our earlier observation that the non-classical selenolo-selenophenes seemed to be more stable than their sulfur analogues,⁷ indicate that selenophenes are generally more stable than the corresponding thiophenes. The structure of **3** was confirmed by its ^1H , ^{13}C and ^{77}Se NMR spectra, as well as by its mass spectrum. The ^1H NMR spectrum is of first order, quite similar to that observed for thieno[3,4-b]thiophene⁶ with well separated signals for all four aromatic protons. Comparison of the chemical shifts of the protons of **3** and thieno[3,4-b]thiophene reveals that the resonances of all the protons occur at lower field for **3**.¹² The most striking difference between the spectra of these two compounds is that the relative positions of the signals attributed to H-4 and H-6 are reversed. As Wynberg *et al.*⁶ did not observe the long-range coupling between H-3 and H-6, this difference could be due to their erroneous assignments of the chemical shifts of H-4 and H-6.

The decoupled ^{13}C NMR spectrum shows as expected six peaks: four of high intensity at δ 131.4 (C-2), 120.7 (C-3), 119.8 (C-4) and 117.9 (C-6) and two of low intensity, as expected for quaternary carbons, at δ 136.9 (C-7) and 152.2 (C-8). The assignments of signals were made from the undecoupled ^{13}C NMR spectrum in analogy with the

assignments for selenolo[2,3-c]thiophene.¹¹ This spectrum is shown in Figure 1. The decoupled ^{77}Se NMR spectrum of **3** shows two peaks, at δ 176.4 (Se-1) upfield from selenophene and δ 126.4 (Se-5) downfield from selenophene, as expected for the unsymmetrical structure of selenolo[3,4-b]selenophene. The assignments of signals were based on the comparison with the ^{77}Se NMR spectrum of selenolo[2,3-c]thiophene¹¹ (δ 173.8 upfield from selenophene), as well as on the analysis of the undecoupled ^{77}Se NMR spectrum, which is shown in Figure 2. The signal at high field is split into two doublets, which is only compatible with the interactions between Se-1 and ring hydrogens H-2 and H-3, giving two different coupling constants $^2J_{\text{Se1-H2}} = 47.1$ Hz and $^3J_{\text{Se1-H3}} = 7.0$ Hz. The magnitude of these coupling constants is also in good agreement with the corresponding coupling constants in **1** and **2**³. The signal at low field is split into a triplet, as expected for the coupling over two bonds between Se-5 and H-4 or H-6. Thus, $^2J_{\text{Se5-H4}} = ^2J_{\text{Se5-H6}} = 48.1$ Hz. This coupling constant can also be obtained from the selenium satellites in the ^1H NMR spectrum. The ^{77}Se couplings to the hydrogens of the adjacent ring are not observed. It should be pointed out that none of the observed selenium signals falls into the ^{77}Se shift region of monosubstituted selenophenes,¹³ although the resonances of both **1** and **2**³ are found there. The great shift difference of 302.8 ppm between Se-1 and Se-5 might be attributed to an appreciable charge separation in the molecule, with Se-5 being the more positively charged of the two selenium atoms. Unfortunately, no calculations of the electron densities in **3** are available but the results of the SCF MO treatment by Dewar *et al.*¹⁴ and of the PPP

calculations by Skancke et al.¹⁵, carried out on thieno[3,4-b]thiophene, indicate a similar charge distribution in this molecule. This is also confirmed by the fact that the resonance of Se-5 is only 6.6 ppm from that of the selenium atom in diphenyl selenoxide,¹⁶ which has a partial positive charge. The resonance of the other selenium atom, Se-1, falls into the region of diarylselenides.¹⁷

There is therefore no doubt, that the selenophene prepared by us has the structure of selenolo[3,4-b]selenophene (3). It is, however, still doubtful that any of the three isomeric selenophenes described by Umezawa² really had the structure of 3. Umezawa's structural assignments were mainly based on dipole moment measurements which were later shown to be erroneous.^{3,18} He had also prepared picrates and tetrabromo derivatives of all three selenophenes. In order to be able to compare all of the data given by Umezawa, we have repeated these experiments on 1-3, and the results are collected in Table 1, together with data given in Ref. 2. The very good agreement of the melting points for 1 and 2 and their derivatives and the striking disagreement of the results obtained for 3 and its derivatives, make it most likely that the compound with b.p. 93-99°C/14 mm Hg described by Umezawa, in spite of the results of the elemental analysis, was not selenolo[3,4-b]selenophene (3). Neither is it easy to believe that 3 would survive the conditions employed in the preparation of selenophene from acetylene and selenium, from which reaction Umezawa claimed isolation of all three selenophenes 1-3. On the other hand, it can now be concluded that both 1 and 2 were, in fact, isolated by Umezawa, though in our preparation of selenophene¹⁹ only selenolo[3,2-b]selenophene (2) was formed.¹

Table 1. Comparison of melting points and assignments of the three isomeric selenoloselenophenes, as reported in Ref. 2 and by present authors

Item	M.p./b.p.		Picrate m.p.		Tetrabromo derivative m.p.		Assignment	
	Ref. 2	Refs. 1, 3 and this work	Ref. 2	This work	Ref. 2	This work	Ref. 2	This work
1	51-51.5 ⁰	56-57 ⁰	154-155.5 ⁰	152-154 ⁰	252.5-253 ⁰	252-254 ⁰	2	1
2	123-124.5 ⁰	127.5-128 ⁰	163-165 ⁰	162-164 ⁰	246-247.5 ⁰	246-248 ⁰	3	2
3	90-93 ⁰ /14mmHg	46-47 ⁰	unstable oil	113 ⁰ (dec.)	271-272 ⁰	*)	1	3

*) 3 decomposes rapidly when brominated with bromine in carbon disulfide under conditions of Ref. 2.

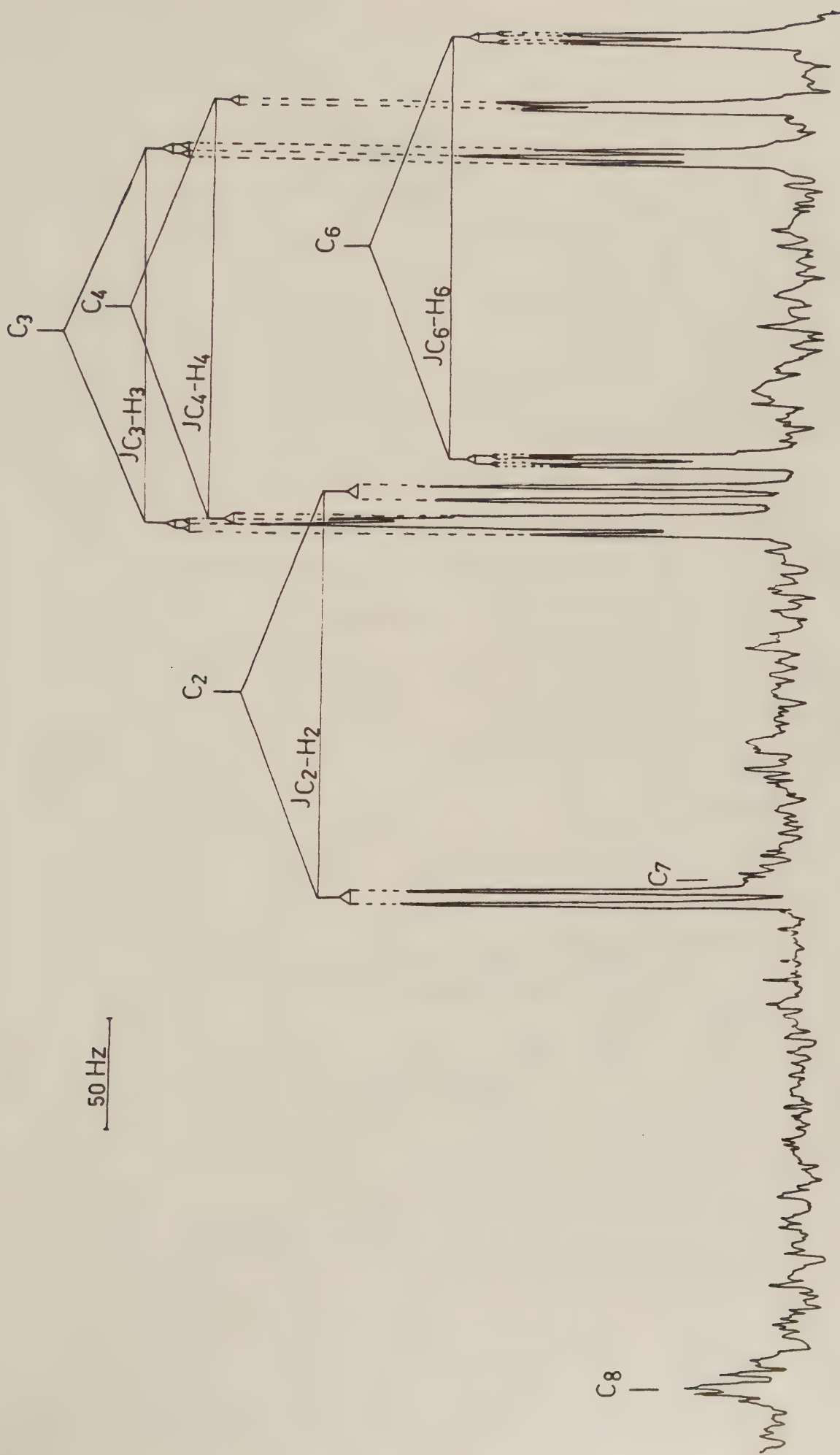
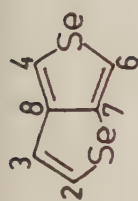


Figure 1. ^{13}C NMR spectrum of selenolo[3,4-b]selenophene in acetone- d_6 at 15.04 MHz

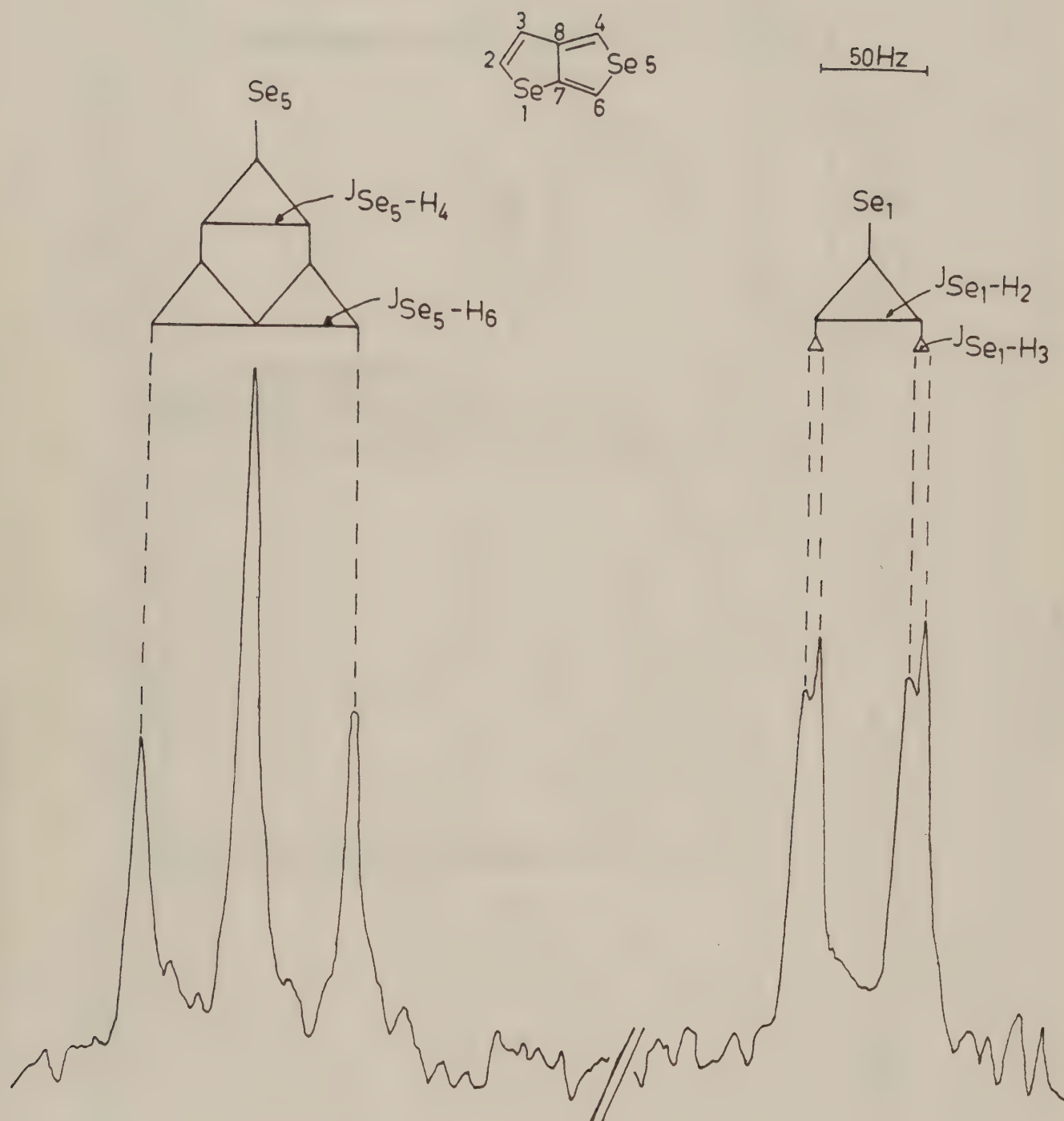


Figure 2. ^{77}Se NMR spectrum of selenolo[3,4-b]selenophene in acetone- d_6 at 19.135 MHz

EXPERIMENTAL

The ^1H NMR spectra were obtained on a JEOL MH 100 high resolution spectrometer. The ^{13}C NMR spectra were obtained at 15.04 MHz with a JEOL JMN-60 spectrometer with a built-in JEOL 980A computer with 12K memory. The ^{77}Se NMR spectra were obtained at 19.135 MHz on a Varian XL-100-15 spectrometer equipped with frequency sweep, proton wide band decoupler and Fourier transform operation. Field-frequency control (lock) was effected by means of the deuterium resonance of hexadeuterioacetone or hexadeuteriodimethyl sulfoxide. Mass spectra were recorded on a Finnigan Model 4021 mass spectrometer and analytical GLC was carried out with a Perkin-Elmer 900 gas chromatograph connected to a Varian 480 digital integrator. The integrator was not calibrated. A Dexil 300 3 % on Chromosorb W AW column was used for all gas chromatographic analyses. The IR spectra were recorded on a Perkin-Elmer 257 instrument. Elementary analyses were carried out by Ilse Beetz, Mikroanalytisches Laboratorium, Kronach, Germany.

2,3-Bischloromethyl-5-carbomethoxyselenophene (4). A solution of 66.2 g (0.35 mol) of 2-carbomethoxyselenophene (b.p.₁₅ 98-99°C, n_{D}^{20} 1.5731; lit.²⁰: b.p.₁₈ 95.5-96°C, n_{D}^{20} 1.5732) in 50 ml of chlorodimethyl ether was added dropwise to a stirred suspension of 47.7 g (0.35 mol) of water-free zinc chloride in 400 ml of chlorodimethyl ether. The temperature rose to about 50°C during the addition. After the addition was complete, the reaction mixture was refluxed for 6 hours. During the first hour of reflux, the colour changed from nearly colourless to deep red. The red solution was then cooled to room temperature and poured onto 800 g of crushed ice, with stirring. After stirring for two hours,

the initially formed light-brown oil solidified.

The solid was removed by filtration, washed with cold water and dried in a rotatory evaporator at 40°C, cooling the receiver in ice. The dried solid was crystallized from petroleum ether (b.p. 40-60°C), which furnished 87.1 g (87 %) of light-yellow needles, m.p. 55-56°C. NMR (CDCl₃): δ 3.87 (s, 3H, CH₃), 4.55 (s, 2H, CH₂), 4.84 (s, 2H, CH₂), 7.98 (s, 1H, H₄). Anal. Calcd. for C₈H₈Cl₂O₂Se: C 33.60; H 2.82; Cl 24.79; Se 27.61. Found: C 33.71; H 2.87; Cl 24.71; Se 27.75.

2-Carbomethoxy-4H,6H-dihydroselenolo[3,4-b]selenophene (5). To a colourless solution of 0.055 mol of sodium hydrogen selenide in 750 ml of abs. ethanol prepared according to Ref. 21, 19.3 g (0.050 mol) of the solid bischloromethyl compound 4 was added in small portions during 5 hours with stirring at room temperature under nitrogen atmosphere. After complete addition, the reaction mixture was stirred overnight at room temperature and the precipitated sodium chloride was filtered off. The filtrate was concentrated to about 200 ml and poured into 1 l of water. The resulting white suspension was extracted with chloroform and then the combined extracts were dried over magnesium sulfate and concentrated, affording 10.3 g (70 %) of a yellow, crystalline residue, the mass spectrum of which indicated the presence of the dimeric compound 6. Separation of the desired product 5 from its dimer 6 could be achieved by fractional crystallization from aqueous ethanol, which gave 1.8 g (12 %) of the dihydroselenophene as light yellow needles, m.p. 85-86°C. NMR (CDCl₃): δ 3.84 (s, 3H, CH₃), 7.71 (s, 1H, H₃) and a strongly coupled AA'BB' spectrum of the methylene protons centred at 4.03

and 4.26. Anal. Calcd. for $C_8H_8O_2Se_2$: C 32.67; H 2.74; Se 53.70. Found: C 32.65; H 2.72; Se 53.66. 7.8 g (53 %) of the dimer **6**, m.p. 227-229°C, was obtained after recrystallization from pyridine/water (9:1). Owing to its low solubility in organic solvents, no NMR spectrum could be recorded. Both the mass spectrum and the elemental analysis were in agreement with the dimeric structure of **6**. In the mass spectrum, the peaks centred at m/e 592 (M^+) and at m/e 296 (base peak), showed the same pattern as a spectrum simulated for four and for two selenium atoms, respectively.

Anal. Calcd. for $C_{16}H_{16}O_4Se_4$: C 32.67; H 2.74; Se 53.70. Found: C 32.67; H 2.89; Se 53.54.

2-Carbomethoxy-4H,6H-dihydroselenolo[3,4-b]selenophene 5-oxide (7).

To a solution of 1.5 g (5.1 mmol) of the selenide **5** in 10 ml of dry tetrahydrofuran, placed at -22°C in the freezing room, a solution of 1.0 g (8.8 mmol) of 30 % hydrogen peroxide in 5 ml of dry tetrahydrofuran was added dropwise with stirring. After stirring overnight at -22°C, the colourless precipitate was filtered off giving 1.1 g of the selenoxide. The filtrate was concentrated in vacuo and filtered to give an additional 0.2 g of the selenoxide, i.e. 82 % yield, m.p. 80-83°C (dec.). All attempts at purification resulted in decomposition. Anal. Calcd. for $C_8H_8O_3Se_2$: C 30.99; H 2.60; Se 50.93. Found: C 31.35; H 2.72; Se 50.03. Due to the low solubility of the selenoxide in $CDCl_3$, $CDBr_3$ and C_6D_6 , the NMR spectrum could only be recorded in $DMSO-d_6$ solution. If the spectrum was recorded immediately after dissolving the compound, the expected signals of the methylene protons appeared as two singlets at δ 3.80 and 3.82, together with a singlet for the

aromatic proton H_3 at δ 7.92 and a singlet at δ 3.86 (s, 3H, CH_3). If, however, the spectrum was recorded after a short period of time the intensity of the methylene signals decreased and the aromatic part of the spectrum indicated formation of the selenolo[3,4-b]selenophene system. Thus, the two α -protons of the selenophene ring appeared at δ 8.81 (d, 1H, H_4) and 8.42 (2d., 1H, H_6) with the coupling constant $J_{H4-H6} = 2.4$ Hz and a long-range coupling to the β -proton of the other ring, $J_{H3-H6} = 0.8$ Hz. This proton gave a signal at δ 8.12 (d, 1H, H_3), and the carbomethoxy group at δ 3.88 (s, 3H, CH_3).

2-Carbomethoxyselenolo[3,4-b]selenophene (8). The selenoxide 7 (1.1 g, 3.5 mmol) was dissolved in 15 ml of acetic anhydride, whereupon a spontaneous exothermic reaction took place and the solution became very dark. After stirring at room temperature for 0.5 hour, the acetic anhydride was hydrolyzed with water, the reaction mixture was extracted with ether and the ether extracts were washed with saturated sodium hydrogen carbonate solution and water, dried over magnesium sulfate and concentrated. Recrystallization of the half-crystalline residue from petroleum ether (b.p. 40-60°C) gave 0.56 g (55 %) of the title compound, m.p. 74-76°C. All spectroscopic data were in accordance with those for 2-carbomethoxyselenolo[3,4-b]-selenophene prepared by esterification of the acid 9 with diazomethane, where the acid was obtained by the independent route (see below) of Scheme 2.

2-Carboxyselenolo[3,4-b]selenophene (9). The ester 8 (0.29 g, 1.0 mmol) was dissolved in 20 ml of 10 % potassium hydroxide solution in methanol and warmed to 50°C for 2 hours, with stirring under nitrogen. After cooling to 0°C, the solution was acidified

with ice-cold 1 N hydrochloric acid and the yellow precipitate was filtered and then recrystallized from acetone. 0.19 g (68 %) of the acid **9** was obtained. All physical and spectroscopic properties were in accordance with those for 2-carboxyselenolo[3,4-b]selenophene prepared by the independent route of Scheme 2 (see below).

Decarboxylation of **9** with copper in quinoline is described below.

4-Bromo-3-methylselenoselenophene. A solution of 70.0 g (0.242 mol) of 3,4-dibromoselenophene²² in 250 ml of dry ether was cooled to -70°C and 159 ml of 1.53 N n-butyllithium (0.243 mol) in hexane diluted with 100 ml of dry ether was added dropwise with stirring under nitrogen at such a rate that the temperature did not exceed -69°C . The addition took one hour and, after stirring for an additional 30 min at -70°C , a solution of 45.1 g (0.240 mol) of dimethyl diselenide in 100 ml of dry ether was added dropwise at -70°C . The reaction mixture was allowed to reach $+5^{\circ}\text{C}$ and was hydrolyzed with 350 ml of ice-cold 2 N hydrochloric acid. After stirring for one hour, the aqueous phase was separated, extracted twice with ether and the combined ethereal solutions washed with sodium hydrogen carbonate solution and water, then dried over magnesium sulfate and concentrated. The dark residue was distilled under nitrogen at 12 mm Hg, giving, after a small fore-run of the starting 3,4-dibromoselenophene, 55.8 g (76.1 %) of the title compound as a light yellow, viscous oil, b.p.₁₂ $159-160^{\circ}\text{C}$.

NMR (CDCl_3): δ 2.32 (s, 3H, $-\text{SeCH}_3$), $J_{\text{Se-CH}_3} = 11.6$ Hz; 7.62 (d, 1H, H_2), 7.93 (d, 1H, H_5); $J_{\text{H}_2-\text{H}_5} = 3.0$ Hz. Assignments of the chemical shifts of the two aromatic protons were based on known substituent-caused shifts. Anal. Calcd. for $\text{C}_5\text{H}_5\text{BrSe}_2$: C 19.82; H 1.66; Se 52.13. Found: C 19.91; H 1.80; Se 52.07.

4-Methylseleno-3-selenophene aldehyde (X). To a solution of 108 ml of 1.53 N n-butyllithium (0.165 mol) in hexane diluted with 100 ml of dry ether was added, dropwise with stirring, 45.4 g (0.150 mol) of 4-bromo-3-methylselenoselenophene in 100 ml of dry ether, under nitrogen at -70°C , at such a rate that the temperature did not exceed -68°C . After an additional 30 min at -70°C , 12.4 g (0.170 mol) of freshly distilled dimethylformamide in 100 ml of dry ether was added dropwise and the reaction mixture was allowed to reach room temperature, then cooled to $+5^{\circ}\text{C}$ and hydrolyzed with 300 ml of ice-cold 2 N hydrochloric acid. After stirring for one hour, the mixture was worked up as in the synthesis of 4-bromo-3-methylselenoselenophene and the very dark residue obtained was fractionated under nitrogen at 1.5 mm Hg, giving 27.2 g (71.9 %) of 4-methylseleno-3-selenophene aldehyde as an orange oil, b.p._{1.5} $141-144.5^{\circ}\text{C}$. Another distillation gave a fraction with b.p._{1.5} $144-144.5^{\circ}\text{C}$, which solidified on standing. The orange solid yielded, after recrystallization from ligroin, fine yellow needles with m.p. $39-40^{\circ}\text{C}$. NMR (CDCl_3): δ 2.30 (s, 3H, $-\text{SeCH}_3$), $J_{77}^{\text{Se-CH}_3} = 12.7$ Hz; 7.50 (2d, 1H, H_5), 9.00 (d, 1H, H_2), 9.91 (d, 1H, CHO), $J_{\text{H}_2-\text{H}_5} = 2.9$ Hz, $J_{\text{H}_5-\text{CHO}} = 0.8$ Hz. These assignments are in good agreement with the published NMR spectrum of 4-methylseleno-3-thiophene aldehyde.²³ Anal. Calcd. for $\text{C}_6\text{H}_6\text{OSe}_2$: C 28.59; H 2.40; Se 62.66. Found: C 28.71; H 2.34; Se 62.71.

2-Carboxyselenolo[3,4-b]selenophene (IX). A mixture of 12.6 g (0.050 mol) of 4-methylseleno-3-selenophene aldehyde, 7.6 g (0.050 mol) of methyl bromoacetate and 7 ml of toluene was heated at 120°C under nitrogen for two days. The toluene was then distilled off under reduced pressure and 40 ml of freshly distilled acetic anhydride and 25 ml of dry

pyridine were added to the dark residue, whereupon the reaction mixture was refluxed under nitrogen for 4 hours. The solvents were then evaporated in vacuo and a solution of 10 g of potassium hydroxide in 70 ml of dry methanol was added to the residue. After two hours of refluxing, the reaction mixture was concentrated to dryness, dissolved in water, filtered, cooled and acidified with diluted hydrochloric acid leaving 8.5 g (61 %) of brown, amorphous solid. Recrystallization from aqueous acetone gave 6.7 g (48 %) of light yellow, glistening crystals, decomposing above 204°C into elemental selenium without melting. NMR (DMSO-d_6): δ 7.81 (d, 1H, H_3), 8.23 (2d, 1H, H_6), 8.69 (d, 1H, H_4), $\text{J}_{\text{H4-H6}} = 2.3$ Hz, $\text{J}_{\text{H3-H6}} = 0.75$ Hz. IR (C=O): 1650 cm^{-1} . Anal. Calcd. for $\text{C}_7\text{H}_4\text{O}_2\text{Se}_2$: C 30.24; H 1.45; Se 56.80. Found: C 30.36; H 1.54; Se 56.91, ^{13}C NMR (DMSO-d_6): δ (ppm) relative to TMS as an internal standard: 139.8 (C-2), 127.1 (C-3), 128.1 (C-4), 120.8 (C-6), 136.0 (C-7), 150.2 (C-8), 165.2 (CO_2H). $^1\text{J}_{\text{C3-H3}} = 170.9$ Hz, $^1\text{J}_{\text{C4-H4}} = 192.9$ Hz, $^1\text{J}_{\text{C6-H6}} = 195.3$ Hz.

2-Carbomethoxyselenolo[3,4-b]selenophene (VIII). Esterification of 280 mg (0.001 mol) of the acid with diazomethane gave 260 mg (89 %) of the methyl ester, m.p. $74-76^{\circ}\text{C}$. NMR (CDCl_3): δ 3.88 (s, 3H, $-\text{CO}_2\text{CH}_3$), 7.82 (d, 1H, H_3), 7.92 (2 $\times$ d, 1H, H_6), 8.15 (d, 1H, H_4); $\text{J}_{\text{H4-H6}} = 2.4$ Hz, $\text{J}_{\text{H3-H6}} = 0.8$ Hz. IR (C=O): 1655 cm^{-1} . Anal. Calcd. for $\text{C}_8\text{H}_6\text{O}_2\text{Se}_2$: C 32.90; H 2.07; Se 54.07. Found: C 33.01; H 1.98; Se 54.24.

Selenolo[3,4-b]selenophene (3). To a solution of 1.40 g (5.0 mmol) of 2-carboxyselenolo[3,4-b]selenophene (9) in 50 ml of freshly distilled quinoline, 0.50 g (7.8 mmol) of copper bronze was added and the mixture heated to 180°C in a nitrogen atmosphere until the calculated volume of carbon dioxide (112 ml) was collected over saturated sodium chloride solution. This took about 0.5 hour, whereupon the quinoline and liquid selenophene were distilled off at reduced pressure, diluted with ether and cooled to 0°C. The colourless solution was then carefully washed with ice-cold 1 N hydrochloric acid holding the temperature at 0°C, as 3 is sensitive to acid. The ether solution was washed with water to neutral pH, dried over magnesium sulfate and concentrated to give 0.85 g (72 %) of a light brown oil, which solidified on cooling. Recrystallization of 3 could be achieved, though with some decomposition, by dissolving it in warm pentane and cooling to -70°C, which gave analytically pure, slightly yellow, glistening crystals, m.p. 46-47°C. NMR (CDCl₃): δ (ppm) 8.03 (d, 1H, H₄), 7.84 (2d, 1H, H₆), 7.78 (d, 1H, H₂), 7.00 (2d, 1H, H₃), $J_{H2-H3} = 6.2$ Hz, $J_{H4-H6} = 2.4$ Hz, $J_{H3-H6} = 0.8$ Hz.

In the mass spectrum, the peaks centred at m/e 236 (M^+ and base peak) showed the same pattern as a spectrum simulated for two selenium atoms. Single-atom selenium patterns were observed at m/e 156 (M^+-Se), m/e 117 (C_3HSe), m/e 105 (C_2HSe) and m/e 93 ($CHSe$).

¹³C and ⁷⁷Se NMR spectra of 3 were described in the text.

Anal. Calcd. for C₆H₄Se₂: C 30.80; H 1.72; Se 67.48.

Found: C 30.94; H 1.81; Se 67.63.

Acknowledgements

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REFERENCES AND NOTES

- ¹S. Gronowitz, A. Konar and A.-B. Hörnfeldt, Chem. Scripta 10, 159 (1976).
- ²S. Umezawa, Bull. Chem. Soc. Japan 14, 363 (1939).
- ³S. Gronowitz, T. Frejd and A.-B. Hörnfeldt, Chem. Scripta 5, 236 (1979).
- ⁴V.P. Litvinov and G. Fraenkel, Izvest. Akad. Nauk SSSR, Ser. Khim. 828 (1968).
- ⁵V.P. Litvinov, A.N. Sukiasyan, Ya.L. Goldfarb and L.V. Bogacheva, Izvest. Akad. Nauk SSSR, Ser. Khim. 1592 (1971).
- ⁶H. Wynberg and D.J. Zwanenburg, Tetrahedron Lett. 761 (1967).
- ⁷S. Gronowitz and A. Konar, J. Chem. Soc., Chem. Commun. 163 (1977).
- ⁸D.J. Zwanenburg, H. de Haan and H. Wynberg, J. Org. Chem. 31, 3363 (1966).
- ⁹C. Paulmier, J. Morel and P. Pastour, Bull. Soc. Chim. France 2511 (1969).
- ¹⁰The 4-bromo-3-selenophene aldehyde ethylene acetal thus obtained was used in our attempts to synthesize the selenophene 3 via the Dieckmann cyclization path used by us in the syntheses of 1 and 2.¹
- ¹¹S. Gronowitz, A. Konar and V.P. Litvinov, Izvest. Akad. Nauk SSSR, Ser. Khim., to be published.
- ¹²This is in accordance with previous investigations on selenophenes and thiophenes, where a stronger shielding in thiophenes is attributed to a more effective lone-pair conjugation of sulfur than of selenium, see J.M. Read, C.T. Mathis and J.H. Goldstein, Spectrochim. Acta 21, 85 (1965).
- ¹³The ⁷⁷Se shifts of 28 monosubstituted selenophenes extend from -95.4 to 112.6 ppm from selenophene, see S. Gronowitz, J. Johnson and A.-B. Hörnfeldt, Chem. Scripta 8, 8 (1975). 1 and 2 give signals at -26.1 and -56.0 ppm (upfield from selenophene) respectively.
- ¹⁴M.J.S. Dewar and N. Trinajstić, J. Am. Chem. Soc. 92, 1453 (1970).

- ¹⁵A. Skancke and P.N. Skancke, Acta Chem. Scand. 24, 23 (1970).
- ¹⁶A. Fredga, S. Gronowitz and A.-B. Hörnfeldt, Chem. Scripta 8, 15 (1975).
- ¹⁷S. Gronowitz, A. Konar and A.-B. Hörnfeldt, Org. Magn. Res. 9, 213 (1977).
- ¹⁸The dipole moment measurements were only carried out on selenolo[3,2-b]-selenophene 2.³
- ¹⁹S. Gronowitz, T. Frejd, A. Moberg-Ogard and L. Tregge, J. Heterocycl. Chem. 13, 1319 (1976).
- ²⁰L. Chierici and L. Pappalardo, Gazz. Chim. Ital. 88, 453 (1958).
- ²¹D.L. Klayman and T.S. Griffin, J. Am. Chem. Soc. 95, 197 (1973).
- ²²C. Dell'Erba, D. Spinelli, G. Garbarino and G. Leandri, J. Heterocycl. Chem. 5, 45 (1968).
- ²³V.S. Bogdanov, V.P. Litvinov, A.N. Sukiasyan and Ya.L. Goldfarb, Zhur. Org. Khim. 7, 1 257 (1971).

Paper G

On the Vilsmeier Formylation and Metalation of Selenolo [2,3-c] thiophene.

On the Vilsmeier Formylation and Metalation of Selenolo[2,3-c]thiophene

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Abstract

On the Vilsmeier formylation and metalation of selenolo[2,3-c]thiophene.

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Chemica Scripta (Sweden)

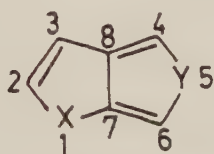
The formylation of selenolo[2,3-c]thiophene (II) gives a mixture of 4- and 6-selenolo[2,3-c]thiophene aldehydes, V and VI, in a ratio of 60:40. Metalation of II with n-butyllithium followed by formylation of the resulting organolithium compounds changes this ratio to 18:82, and in addition gives a product of a ring-opening reaction of a substitutional RO II-type (VII). This is the first example of the cleavage of the C-Se bond between a selenium atom and a β -carbon of a thiophene ring.

^1H , ^{13}C and ^{77}Se NMR of II and some of its derivatives were recorded and are discussed in the article.

Introduction

Thieno[3,4-b]thiophene (I) was synthesized in 1967 by Wynberg and Zwanenburg [1], and shown to be an unstable colourless oil.

Its selenium-containing analogue II was reported four years later by Litvinov et al. [2] as a stable, crystalline compound with m.p. 25°C. Some preliminary results [3] indicate however, that the other selenium analogue, selenolo[3,4-b]thiophene (III) resembles the thiophene I in its instability, although selenolo[3,4-b]selenophene (IV) is a quite stable crystalline compound with m.p. 46-7°C [4].



I X = S , Y = S

II X = Se, Y = S

III X = S , Y = Se

IV X = Se, Y = Se

Wynberg et al. [5] had also carried out some substitution reactions on I, and found that both electrophilic attack and metalation take place at positions 4 and 6, which was in accordance with predictions based on quantum chemical calculations. Both calculations of electron densities and semiempirical methods with all valence electrons predict the 4- and 6-positions in I to be the most reactive towards electrophilic and nucleophilic substitution.

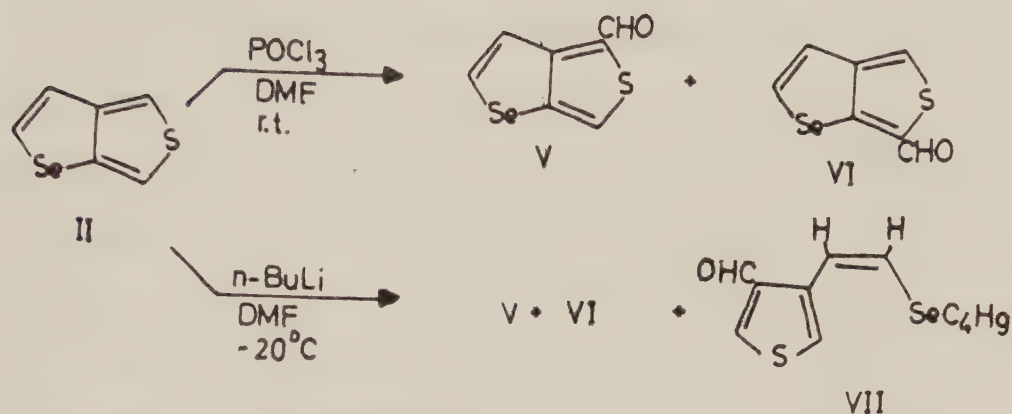
(For a review of quantum chemical calculations and reactivities of the isomeric thienothiophenes, see Ref. 6 and references therein.)

The reactions carried out by Wynberg et al. [5] on I were Vilsmeier formylation and metalation with n-butyllithium. Formylation gave a mixture of the 4- and 6-formyl derivatives in a ratio of 70:30, whereas a reversal of the product ratio (20:80) was observed on metalation at -20°C . These two reactions were also carried out on the 2-methoxycarbonyl derivative of I, but there is no report in the literature of any substitution reactions of selenolo[2,3-c]thiophene (II), although a review concerning syntheses and physical properties of the isomeric selenolothiophenes has appeared [7].

Results and Discussion

Selenolo[2,3-c]thiophene (II) was synthesized according to Ref. 2 and characterized by its melting point, mass spectrum and ^1H NMR spectrum, which was in full accord with that given by Litvinov et al. [7]. We have also measured its ^{13}C and ^{77}Se NMR spectra, for which the chemical shifts and coupling constants are given in Tables I and II, together with the data for some other derivatives of II. The assignments of signals in these spectra will be discussed later. In order to be able to compare the results obtained with those for thieno[3,4-b]thiophene (I), we have carried out Vilsmeier formylation and n-butyllithium metalation of II, i.e. the same reactions and under the same experimental conditions as

Wynberg et al. [5]. The results are summarized in the following scheme (Scheme I):



Scheme I

Vilsmeier formylation gave a mixture of 4-selenolo[2,3-c]thiophene aldehyde (V) and 6-selenolo[2,3-c]thiophene aldehyde (VI) in a ratio of 60:40. This ratio was determined independently by gas chromatography and by NMR spectroscopy, since the resonances of the aldehydic protons of V and VI were well separated. The overall yield of the reaction was 70 %, and the separation of the two aldehydes was achieved by flash chromatography [8], which very conveniently gave the pure samples of V and VI already after one run.

Metalation of selenolo[2,3-c]thiophene (II) at -20°C using 1 equivalent of n-butyllithium, followed by formylation of the resulting organolithium compound also led to the mixture of the 4- and 6-substituted isomers V and VI, and in addition the product of a ring-opening reaction (VII). VII was actually a main product of the reaction, isolated in 42 % yield. The isolated yield of the two aldehydes V and VI was 30 % and the ratio of V:VI = 18:82.

Again this ratio and the relative amount of VII could be determined independently by gas chromatography and NMR spectroscopy, since the resonances of all three aldehydes were well separated. Separation of the crude product mixture after metalation was achieved by means of flash chromatography and gave pure samples of VI and VII, along with traces of the 4-substituted aldehyde V.

The results of Vilsmeier formylation and metalation of II are in very good agreement with those obtained by Wynberg *et al.* [5] for thieno[3,4-*b*]thiophene (I), both regarding the preferential sites of an electrophilic attack and the ratios of the products formed. The results are also in agreement with the recent calculations of Litvinov *et al.* [9], who performed a quantum chemical analysis of all isomeric thienothiophenes, selenolothiophenes and selenolo-selenophenes by using the semiempirical LCAO SCF MO method, including all valence electrons - CNDO/2. The reactivities were estimated from the energy of localization Λ^+ , and Figure 1 shows the values of $\Delta\Lambda^+$ relative to the 3-position of thiophene, for the compounds I-IV.

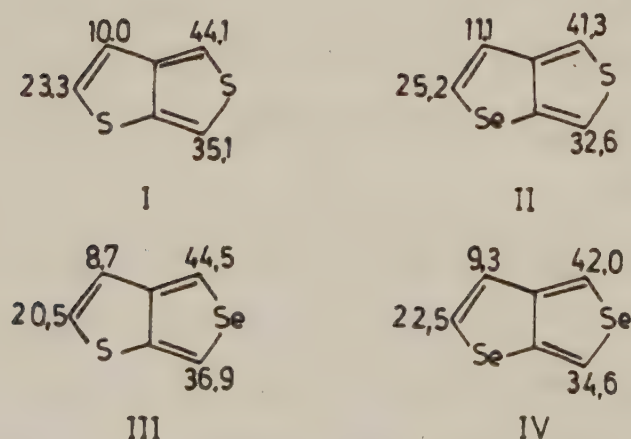
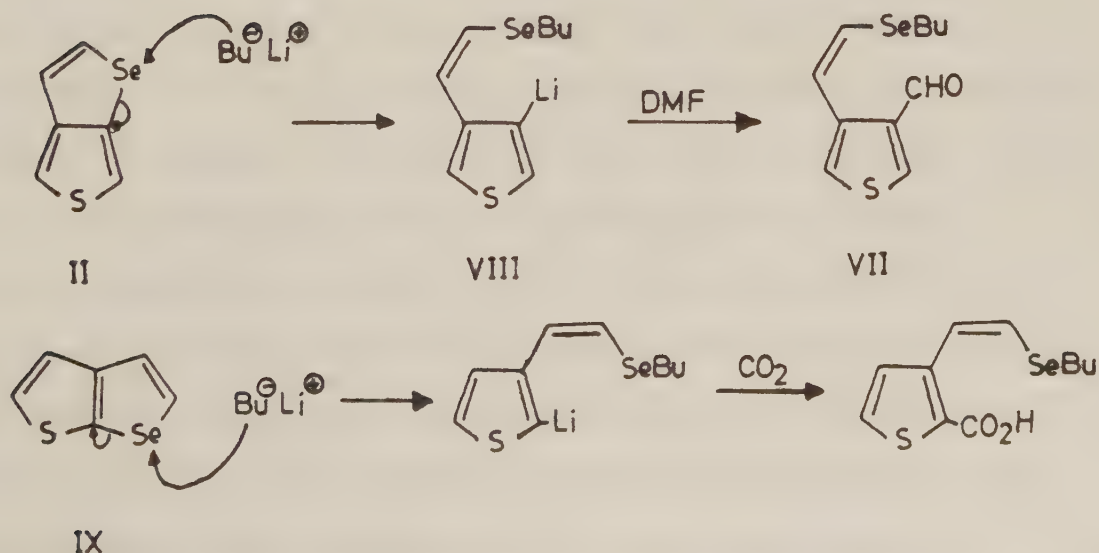


Figure 1

The somewhat greater amount of 4- than 6-substituted product formed in Vilsmeier formylation is thus in agreement with the above figures. Reversal of product ratios on going from electrophilic substitution to metalation may be rationalized by the possible coordination of the lithium atom in the 6-position with either the adjacent selenium or sulfur atom.

It can thus be concluded that selenolo[2,3-c]thiophene (II) behaves very much like thieno[3,4-b]thiophene (I) on electrophilic substitution and on metalation, with the exception of the ring-opening reaction to give VII. In view of the several ring-opening reactions of selenophenes discovered during the past few years (for review, see Ref. 10 and references therein), the ring-opening of II was however not unexpected.

According to the classification proposed by Gronowitz and Frejd [10], the ring-opening of II is of the substitutional RO II-type, and its mechanism can thus be written as in Scheme II, where the similar ring-opening of selenolo[2,3-b]thiophene (IX) is also shown.



Scheme II

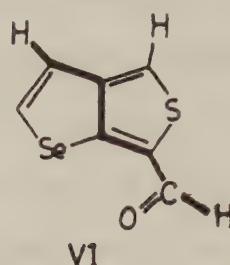
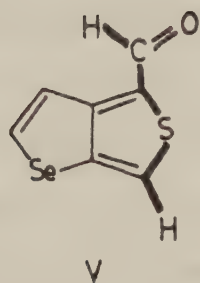
Much less is known about this type of substitutional ring-opening reaction than about the eliminative ring cleavage, but recently some fused selenophenes [11,12], 2,5-diphenyltellurophene [13], benzo[b]thiophene [14] and even some suitably substituted non-fused selenophenes [15] have been shown to undergo this type of reaction. In the most similar case, *i.e.* ring-opening of the selenolo[2,3-b]thiophene (IX) [12], the intermediate is a 2-thienyllithium derivative, whereas in the case of II, one obtains a cleavage of the C-Se bond between the β -position of the thiophene ring and the selenium atom, with the resulting 3-thienyllithium derivative VIII as an intermediate (see Scheme II). We observed no subsequent ring-opening reaction of VIII, which, as a 3-thienyllithium derivative, would probably undergo an eliminative ring fission under more forcing conditions. It is known [16] that the [3,2-b]-annelated isomer of IX, namely selenolo[3,2-b]thiophene, is attacked by butyllithium in both α -positions in a normal way and does not undergo any ring-opening reaction. Neither benzo-selenolo[3,2-b]thiophene or -selenophene are cleaved by *n*-butyllithium, in contrast to their [2,3-b]-annelated analogues [11]. The differentiation between these two isomers was later attempted by means of CNDO/2-3R calculations and by means of studying their ^{77}Se NMR spectra [17]. It was concluded that the vicinity of the heteroatoms in the "cis" compounds increases the ring strain in these molecules, which is known [10] to increase the tendency for reaction of the R0 II-type. In the "trans" compounds, the steric ring inhibitions were assumed to be less effective due to relative positions of the heteroatoms. If we assume the ring strain to be a main factor responsible for the cleavage of the carbon-selenium bond in the "cis" compounds, then the type of annelation

present in selenolo[2,3-c]thiophene (II) obviously gives rise to ring strain more similar to that in selenolo[2,3-b]thiophene (IX) than in its "trans"-isomer.

NMR spectra and Assignments of Signals

As already mentioned, the ^1H NMR spectrum of selenolo[2,3-c]thiophene (II) was in full accord with that given in Ref. 7, being a first order spectrum with well separated signals for all four aromatic protons. The ^1H NMR spectra of the two aldehydes V and VI were quite similar to those for their sulfur analogues, described by Wynberg et al. [5]. Both showed a coupling constant of 6.0 Hz, characteristic for an α - β coupling in selenophenes, and indicating that substitution had taken place exclusively in the 4- and 6-positions, i.e. in the thiophene part of the molecule. This coupling is not present in the spectrum of 2-carboxyselenolo[2,3-c]thiophene (X), where instead a coupling between the 4- and 6-protons can be observed (2.8 Hz). In the spectrum of the 4-substituted aldehyde V, the aldehyde resonance appeared as a doublet with coupling constant of 0.6 Hz, whereas the aldehyde signal of the 6-substituted compound VI was a sharp singlet. This was also the case for the sulfur analogues of V and VI, where the splitting of the aldehydic proton in 4-thieno[3,4-b]thiophene aldehyde was established by means of the decoupling experiments to be due to the long-range coupling over 5 bonds with H_6 [5]. Since such long-range couplings in condensed heterocyclic systems are known to be transmitted along a regular zig-zag path [6], this means that V and VI preferentially exist in the S-cis

and S-trans (but Se-cis) forms, respectively, as shown below.



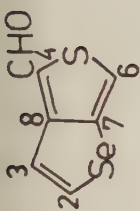
The long-range coupling in VI through 6 bonds is however too small to be observed. Moreover, these facts also confirm the suggestion of Gronowitz et al. [18] that the 2-carbonyl selenophene derivatives preferentially exist in the Se-cis form, probably due to the attractive binding interaction between the carbonyl oxygen lone-pair and the selenium d-orbitals. A brief inspection of Table I, containing the ^{77}Se NMR shifts of V and VI, reveals an anomalously large upfield shift for the selenium atom in the 6-aldehyde, compared to both the 4-aldehyde and the unsubstituted selenolo[2,3-c]thiophene (II), which again corroborates the above suggestion.

The ^{77}Se NMR shifts for II, V, VI and 2-carboxyselenolo[2,3-c]thiophene (X) are given in Table I, relative to selenophene and to II itself. The decoupled spectra of all four compounds show only one signal in the region 152.2 to 211.3 ppm upfield from selenophene. This is not the ^{77}Se shift region of monosubstituted selenophenes [18], wherein lie the resonances of selenolo[2,3-b]thiophene [19], selenolo[3,2-b]thiophene [20], and the isomeric selenophthenes [21,22], but rather the region of diarylselenides [23]. This suggests an appreciable charge separation in the [2,3-c]-fused selenolothiophene and its derivatives, with the sulfur atom being more positively charged than the selenium atom.

In Table II, the ^{13}C NMR data for selenolo[2,3-c]thiophene (II), the aldehydes V and VI and the acid X are collected. Only the direct coupling constants $^1J_{\text{CX-HX}}$ are given, the long-range couplings varying between 3.7 Hz for $^3J_{\text{C4-H6}}$ and 7.3 Hz for $^2J_{\text{C2-H3}}$. In all cases, hexadeuterioacetone was used as solvent, and the shifts were determined from proton decoupled spectra using TMS as an internal standard. Assignments of signals were facilitated by the fact that we could compare the NMR data for the three derivatives of selenolo[2,3-c]thiophene (II) with different substitution patterns, *i.e.* 2-, 4- and 6-substitution. As an example, the ^{13}C NMR spectrum of 4-selenolo[2,3-c]thiophene aldehyde (V) is given in Figure 1.

C-7 and C-8, as well as the substituent carbon, were identified by their lower intensity, as expected for quaternary carbons due to their relatively longer relaxation times. Because of the asymmetry of the parent system II, the absorptions of C-7 and C-8 are not equivalent, and were assigned by comparison with ^{13}C NMR spectra of thieno[2,3-b]thiophene [23]. It is known [24] that α -carbons of thiophene absorb at higher field than β -carbons (a difference of 1.7 ppm). This effect is much more pronounced in thieno[2,3-b]thiophene [23], where C-7, *i.e.* the bridged carbon situated α in both thiophene rings, absorbs 10.3 ppm upfield from C-8, and even more in selenolo[2,3-b]selenophene [21], the difference there being 14.2 ppm. In II, the C-7 carbon is situated α in selenophene and β in the thiophene ring, and C-8 carbon β in both rings. On these grounds, we have assigned the most downfield quaternary carbon in II and all of its derivatives to C-8, and the other one, absorbing at higher field, to C-7.

It is also known that the direct coupling between ring carbons and their hydrogens is greater for α - than for β -carbons, which facilitated assignment of C-3 - the only β -carbon in II and its derivatives. The remaining assignments of the α -carbons C-2, C-4 and C-6 were done on the following grounds. The absorption of C-2, which is located in the selenophene part of the molecule, always occurs at lower field than of the thiophene carbons C-4 and C-6. The differentiation between them was effected by means of the comparison of the direct coupling constants which are always greater for C-6 than for C-4.



100 Hz

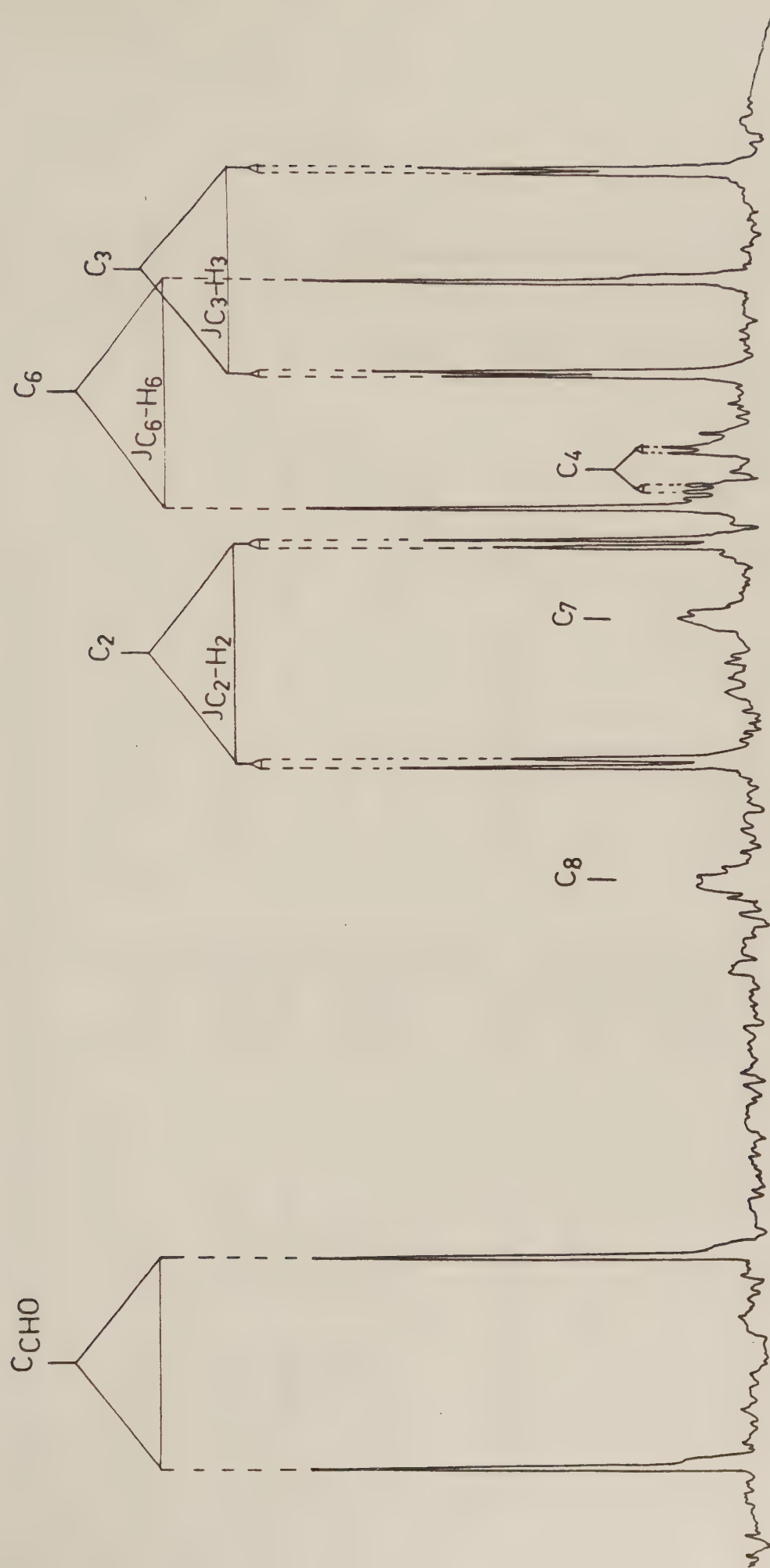


Figure 1. ^{13}C NMR spectrum of 4-selenolo[2,3-c]thiophene aldehyde in acetone- d_6 at 15.04 MHz

Table I

^{77}Se NMR chemical shifts for selenolo[2,3-c]thiophene (II) and some of its derivatives in deuterioacetone solution at 19.135 MHz using selenophene as an external standard

	$\Delta\text{Se}^{\text{a}}$ relative to	
	Selenophene	II
II	-173.8	0
V	-152.2	21.6
VI	-211.3	-37.5
x^{b}	-166.0	7.8

a $\Delta\text{Se} = \text{Se}(\text{substrate}) - \text{Se}(\text{reference})$; positive values are downfield.

b In acetone- d_6 /dimethyl sulfoxide- d_6 (3:1) solution.

Table II. ^{13}C NMR chemical shifts for selenolo[2,3-*c'*]thiophene and some of its derivatives in deuterioacetone solution at 15.04 MHz using TMS as an internal standard

	δ (ppm)	C_2	C_3	C_4	C_6	C_7	C_8	$\text{C}=\text{O}$
II	δ (ppm)	133.0(186.8) ^a	120.8(172.1)	114.9(188.0)	115.2(192.9)	136.4	150.7	
V	δ (ppm)	141.6(186.8)	120.0(172.1)	131.2	126.9(192.9)	139.7	154.6	181.6(178.2)
VI	δ (ppm)	135.5(186.8)	120.0(172.1)	126.5(189.2)	130.2	139.3	151.2	181.0(177.0)
χ ^b	δ (ppm)	140.7	126.5(170.9)	120.3(190.4)	115.9(194.1)	135.5	147.6	164.8

^a Figures within parentheses refer to the direct coupling constants $^1J_{\text{CX-HX}}$ in Hz.

^b In acetone- d_6 /dimethyl sulfoxide- d_6 (3:1) solution.

Experimental

The ^1H NMR spectra were obtained on a JEOL MH 100 high resolution spectrometer. The ^{13}C NMR spectra were obtained at 15.04 MHz on a JEOL JMN-60 spectrometer with a built-in JEOL 980A computer with 12K memory. The ^{77}Se NMR spectra were obtained at 19.135 MHz on a Varian XL-100-15 spectrometer equipped with frequency sweep, proton wide band decoupler and Fourier transform operation. Field-frequency control (lock) was effected by means of the deuterium resonance of hexadeuterioacetone or hexadeuteriodimethyl sulfoxide. Mass spectra were recorded on a Finnigan Model 4021 mass spectrometer, and analytical GLC was carried out with a Perkin-Elmer 900 gas chromatograph connected to a Varian 480 digital integrator. The integrator was not calibrated. A Dexil 300 3 % on Chromosorb W AW column was used for all gas chromatographic analyses. Elementary analyses were carried out by Ilse Beetz, Mikroanalytisches Laboratorium, Kronach, Germany.

Selenolo[2,3-c]thiophene (II). Selenolo[2,3-c]thiophene (II) was prepared by the method of Litvinov et al. [2]. Its ^1H NMR spectrum was in perfect agreement with that given in Ref. 7. The ^{13}C and ^{77}Se NMR spectra in 20 % hexadeuterioacetone solution were recorded and are discussed in the text. The chemical shifts and coupling constants are given in Tables I and II.

Vilsmeier formylation of selenolo[2,3-*c*]thiophene (II). A solution of 936 mg (5.0 mmol) of II in 10 ml of dimethylformamide (DMF) was cooled to 0°C and a solution of 1.0 g (6.5 mmol) of POCl₃ in 5 ml of DMF was added dropwise with stirring under a nitrogen atmosphere. After addition was complete, the solution was stirred for one hour at room temperature, and then poured into 150 ml of 1 N sodium hydroxide. The resulting yellow suspension was extracted with ether, and the combined ether extracts were washed with water and dried over magnesium sulfate. Evaporation of the solvent left 820 mg of a dark brown oil, which was analyzed by means of combined gas chromatography and mass spectrometry, and ¹H NMR spectroscopy. GLC analysis of the crude oil showed it to consist of the unreacted selenolo[2,3-*c*]thiophene (II) (13 %), 4-selenolo[2,3-*c*]thiophene aldehyde (V) (51 %), and 6-selenolo[2,3-*c*]thiophene aldehyde (VI) (34 %), i.e. the ratio of 4- and 6-substituted aldehydes was 60:40. Integration of the aldehyde signals of V (δ 10.02) and VI (δ 9.89) gave exactly the same ratio of V:VI. The crude reaction product was then subjected to flash chromatography [8] on 230-400 mesh silica gel using a mixture of ethyl acetate and petroleum ether (1:4) as eluent. After one run on a 50 mm column, we obtained 75 mg (8 %) of the unreacted II, 250 mg (23 %) of pure V, 429 mg (40 %) of a mixture of V and VI and 74 mg (7 %) of pure VI, i.e. the overall yield of the reaction was 70 %, or 76 % based on reacted selenolo[2,3-*c*]thiophene.

The fractions containing a mixture of V and VI were chromatographed once more under the same conditions, giving an additional 160 mg of V and 45 mg of VI.

4-Selenolo[2,3-c]thiophene aldehyde (V). An analytical sample of V was obtained after crystallization from ligroin as yellow needles, m.p. 108-110°C. NMR (CDCl₃): δ (ppm) 7.70 (2Xd, 1H, H₃), 7.74 (broad singlet, 1H, H₆), 8.19 (d, 1H, H₂), 10.02 (d, 1H, CHO); $J_{H2-H3} = 6.0$ Hz, $J_{H3-H6} = 0.6$ Hz, $J_{H6-CHO} = 0.6$ Hz. Calc. for C₇H₄OSse: C 39.08; H 1.87; S 14.90; Se 36.70. Found: C 39.01; H 1.84; S 14.14; Se 36.08.

6-Selenolo[2,3-c]thiophene aldehyde (VI). An analytical sample of this yellow compound (m.p. 47-49°C) was obtained after crystallization from petroleum ether (b.p. 60-80°C). NMR (CDCl₃): δ (ppm) 7.22 (d, 1H, H₃), 7.81 (s, 1H, H₄), 7.91 (d, 1H, H₂), 9.89 (s, 1H, CHO); $J_{H2-H3} = 6.0$ Hz. Calc. for C₇H₄OSse: C 39.08; H 1.87; S 14.90; Se 36.70. Found: C 38.89; H 1.91; S 15.02; Se 37.12.

Metalation of selenolo[2,3-c]thiophene II. A solution of 936 mg (5.0 mmol) of II in 20 ml of dry ether was cooled to -20°C and a solution of 3.5 ml of 1.44 N *n*-butyllithium in hexane diluted with 5 ml of dry ether was added dropwise with stirring under a nitrogen atmosphere. The solution became dark yellow. After the addition, the reaction mixture was stirred for 20 min at -20°C, whereupon 365 mg (5 mmol) of dimethylformamide was added dropwise. The mixture was then stirred for 30 min at room temperature and poured into 150 ml of 1 N hydrochloric acid. The organic layer was separated and the water layer extracted with ether. The combined organic phases were washed with saturated sodium hydrogen carbonate solution and water, and dried over magnesium sulfate. Evaporation of the solvent gave 970 mg of a dark brown oil, which was analyzed analogously to the crude

reaction product of Vilsmeier formylation. The composition of the product mixture was thus shown to be as follows: unreacted selenolo[2,3-c]-thiophene (II) 15 %, 4-selenolo[2,3-c]thiophene aldehyde (V) 7 %, 6-selenolo[2,3-c]thiophene aldehyde (VI) 32 %, and 4-(β -butylselenoethenyl)thiophene-3-aldehyde (VII) 45 %, which means the ratio of 4- and 6-substituted aldehydes is 18:22. The same ratio was obtained by integration of the aldehyde signals of V and VI. This measurement was possible since the well separated resonance of the aldehyde proton in VII lies between those of V and VI (δ 9.97). Flash chromatography of the reaction mixture under the same conditions as above afforded (after one run) 120 mg (13 %) of the unreacted II, 150 mg (14 %) of the mixture of V and VI, 175 mg (16 %) of pure VI and 575 mg (42 %) of pure VII, i.e. the overall yield of the reaction was 72 %, or 83 % based on reacted selenolo[2,3-c]thiophene.

4-(β -Butylselenoethenyl)thiophene-3-aldehyde (VII). The structure of VII, which was a red, viscous liquid, was confirmed by its mass spectrum, ^1H and ^{13}C NMR spectra and elemental analysis. In the mass spectrum, the peaks centred at m/e 274 (M^+) showed the same pattern as a spectrum simulated for one selenium and one sulfur atom. The base peak was observed at m/e 137 ($M^+ - \text{SeC}_4\text{H}_9$). NMR ($(\text{CD}_3)_2\text{CO}$): δ (ppm) 0.83 (t, 3H, CH_3), 1.27-1.85 (m, 4H, $2\times\text{CH}_2$), 2.87 (t, 2H, $-\text{SeCH}_2-$), 6.89 (d, 1H, H_2), 7.56 ($2\times$ d, 1H, H_5), 7.61 (d, 1H, H_β), 8.42 (d, 1H, H_2), 9.97 (d, 1H, CHO); $J_{\text{H}_2-\text{H}_5} = 3.0$ Hz, $J_{\text{CHO}-\text{H}_5} = 0.8$ Hz, $J_{\text{H}_\alpha-\text{H}_\beta} = 10.5$ Hz, $J_{\text{CH}_2-\text{CH}_3} = 7.0$ Hz. ^{13}C NMR ($(\text{CD}_3)_2\text{CO}$): δ (ppm) relative to TMS as an internal standard: 13.8 (CH_3), 23.3 ($\text{CH}_2-\gamma$), 25.9 ($\text{CH}_2-\beta$), 33.7 ($\text{CH}_2-\alpha$), 122.4 (C_α), 125.5 (C_5), 126.9 (C_β), 138.3 (C_4), 140.7 (C_3), 141.2 (C_2), 186.6 (C_{CHO}). $^1J_{\text{C}_\alpha-\text{H}_\alpha} = 163.6$ Hz, $^1J_{\text{C}_\beta-\text{H}_\beta} = 175.8$ Hz, $^1J_{\text{C}_5-\text{H}_5} = 185.6$ Hz, $^1J_{\text{C}_2-\text{H}_2} = 188.0$ Hz,

$^1J_{\text{CCHO-HCHO}} = 175.8 \text{ Hz. Calc. for } C_{11}H_{14}OS\text{Se: C } 48.35; \text{ H } 5.16; \text{ S } 11.73;$
 $\text{Se } 28.90. \text{ Found: C } 48.97; \text{ H } 5.37; \text{ S } 11.79; \text{ Se } 28.89.$

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References

1. Wynberg, H. and Zwanenburg, D.J., Tetrahedron Letters 1967, 761.
2. Litvinov, V.P., Sukiasyan, A.N., Goldfarb, Ya.L. and Bogacheva, L.V.,
Izvest. Akad. Nauk SSSR, Ser. chim. 1971, 1592.
3. Konar, A. and Gronowitz, S., to be published.
4. Konar, A. and Gronowitz, S., Tetrahedron, submitted for
publication.
5. Wynberg, H. and Feijen, J., Rec. Trav. Chim. Pays-Bas 1970, 89, 77.
6. Litvinov, V.P. and Goldfarb, Ya.L., Advan. Heterocycl. Chem.
1976, 19, 123.
7. Litvinov, V.P., Goldfarb, Ya.L., Bogdanov, V.S., Konjaeva, I.P.
and Sukiasyan, A.N., J. prakt. Chem. 1973, 315, 850.
8. Still, W.C., Kahn, H. and Mitra, A., J. Org. Chem. 1978, 43, 2923.
9. Abronin, I.A., Litvinov, V.P., Zhidomirov, G.M., Djumanazarova, A.Z.
and Goldfarb, Ya.L., Khim. Geterots. Soedin. 1980, No. 2, in press.
10. Gronowitz, S. and Frejd, T., Khim. Geterotsikl. Soedin. 1978, 435.
11. Iteke, F.B., Christiaens, L. and Renson, M., Tetrahedron 1976, 32, 689.
12. Litvinov, V.P., Konjaeva, I.P. and Goldfarb, Ya.L.,
Izvest. Akad. Nauk SSSR, Ser. Khim. 1976, 477.
13. Luppold, E., Müller, E. and Winter, W., Z. Naturforsch. 1976, 31B, 1654.
14. Bayer, A.E.M. and Kloosterziel, H., Recueil, J. Roy. Netherl. Chem.
Soc. 1977, 96, 178.
15. Gronowitz, S., Hallberg, A. and Frejd, T., Tetrahedron 1979, 35, 2607.
16. Litvinov, V.P., Konjaeva, I.P. and Goldfarb, Ya.L., Izvest. Akad. Nauk
SSSR, Ser. Khim. 1974, 1575.
17. Baiwir, M., Llabrès, G., Piette, J.-L. and Christiaens, L.,
Org. Magn. Res., in press.

18. Gronowitz, S., Johnson, I. and Hörnfeldt, A.-B., *Chemica Scripta* 1975, 8, 8.
19. Christiaens, L., Piette, J.-L., Laitem, L., Baiwir, M.,
Denoel, J. and Llabres, G., *Org. Magn. Res.* 1976, 8, 354.
20. Konar, A., unpublished results.
21. Gronowitz, S., Konar, A. and Hörnfeldt, A.-B., *Chemica Scripta* 1976, 10, 159.
22. Gronowitz, S., Frejd, T. and Hörnfeldt, A.-B., *Chemica Scripta* 1974, 5, 236.
23. Gronowitz, S., Johnson, I. and Bugge, A., *Acta Chem. Scand.* 1976,
B 30, 417.
24. Page, T.F., Alger, T. and Grant, D.M., *J. Am. Chem. Soc.* 1965, 87, 5333.

Paper H

Nonclassical Selenoloselenophenes.

Nonclassical Selenoloselenophens

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Nonclassical Selenoloselenophens

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(Division of Organic Chemistry 1, Chemical Center, University of Lund, P.O. Box 740, S-220 07 Lund, Sweden)

Summary Evidence for the existence of nonclassical selenoloselenophens, the 4,6-dimethyl- and 4,6 diethoxy-carbonylselenolo[3,4-*c*]selenophens (**1b**) and (**1c**), which appear to be more stable than the corresponding thieno[3,4-*c*]thiophens, has been obtained.

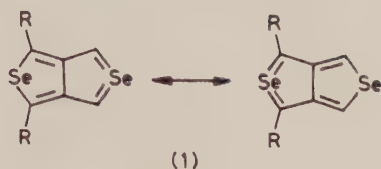
We report some results concerning syntheses of the first derivatives of the selenolo[3,4-*c*]selenophene system (**1**) for which the only uncharged resonance contributors are structures containing tetravalent selenium in one of the rings. Derivatives of the corresponding sulphur-containing system, thieno[3,4-*c*]thiophen, were earlier reported by Cava *et al.*¹

Chloromethylation of 2,5-dimethylselenophen² gave (89%) yellow needles of (**2a**), m.p. 71.5–73 °C. The Hinsberg reaction of dimethyl selenodiacetate and biacetyl followed

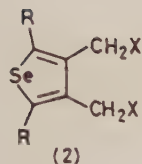
by esterification of the acid and bromination with *N*-bromosuccinimide afforded in 34% overall yield yellow needles of (**2b**), m.p. 147–148 °C. Both (**2a**) and (**2b**) were cyclized with ethanolic sodium hydrogen selenide to give mixtures of (**3a**) and (**4a**), and of (**3b**) and (**4b**). Separation was achieved by steam distillation to give colourless prisms of (**3a**) (45%, m.p. 87–88 °C) and yellow needles of (**3b**) (88%, m.p. 111–113 °C).

Periodate oxidation³ of (**3a**) and (**3b**) gave the selenoxides (**5a**) (86%, m.p. 97–99 °C) and (**5b**), and bromination with bromine in carbon tetrachloride⁴ gave the dibromides (**5c**) (94%, m.p. 118–120 °C) and (**5d**) (92%, m.p. 149–151 °C).[†] Compound (**5a**) decomposed on the attempted crystallization from benzene, and when its solution in acetic anhydride was heated to reflux under nitrogen, an intense red-violet fluorescent colour developed

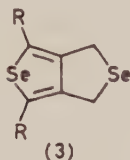
[†] Satisfactory elemental analyses have been obtained for compounds (**2a**), (**2b**), (**3a**), (**3b**), (**4a**), (**4b**), (**5a**), (**5c**), and (**5d**).



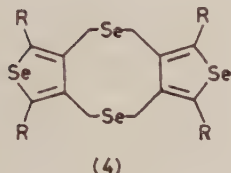
- (1)
 a, R = H
 b, R = Me
 c, R = CO₂Et



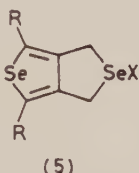
- (2)
 a, R = Me; X = Cl
 b, R = CO₂Me; X = Br



- (3)
 a, R = Me
 b, R = CO₂Et



- (4)
 a, R = Me
 b, R = CO₂Et



- (5)
 a, R = Me; X = O
 b, R = CO₂Et; X = O
 c, R = Me; X = Br₂
 d, R = CO₂Et; X = Br₂

rapidly. This colour, which we attribute to the selenolo-selenophen (**1b**), remained unchanged after an additional 3 h of refluxing. We could not, however, isolate this violet product, owing to its sensitivity to air, but in a similar dehydration in the presence of *N*-phenylmaleimide (NPM), where the violet colour disappeared after 1 h, we were able to trap the selenoloselenophen (**1b**) as its NPM adduct.

Compound (**5b**) could not be isolated in the pure state, as the extraction of its colourless methanol-water solution with any water-immiscible organic solvent gave the deep violet fluorescence of the organic-phase extracts. This colour, which we attribute to the selenoloselenophen (**1c**), developed fastest when benzene was used as a solvent and remained unchanged during 5 h. When a solution of NPM in benzene was added, the violet colour disappeared within 5 min and a few crystals of the NPM adduct precipitated. The compositions of both adducts were confirmed by their mass spectra.

When the extraction of the selenoxide (**5b**) solution was carried out with *n*-hexane, a u.v. spectrum of the violet hexane solution showed λ_{max} 563 nm. Extraction with C₆D₆ allowed us to record the n.m.r. spectrum of the violet benzene solution, which showed a single peak at δ 10.04 (aromatic H), which disappeared after 0.5 h.

The dibromides (**5c**) and (**5d**) were decomposed within a few minutes when stirred with 40% NaOH at 0 °C under nitrogen. When the resulting milky emulsions were stirred with hexane, (**1b**) and (**1c**) respectively, were slowly released into the organic phase (much faster when stirred with benzene); this process was followed by the appearance of a deep violet colour remaining for > 2 h in the case of (**1b**) and 5 h with (**1c**), indicating that the selenolo[3,4-*c*]-selenophen derivative substituted by electron-withdrawing groups is more stable than that substituted by electron-donating groups.

Upon attempted isolation of (**1b**) and (**1c**) in the pure state, the selenides (**3a**) and (**3b**) along with some polymeric materials were obtained. The violet colour disappeared in both cases during 5–10 min when an NPM solution in benzene was added, giving the same NPM adduct as described above. Our preliminary results also indicate that nonclassical selenoloselenophen compounds might be more stable than the corresponding sulphur ones,¹ which is somewhat unexpected considering the results obtained with selenabenzenes.⁶

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¹ M. P. Cava and M. V. Lakshmikantham, *Accounts Chem. Res.*, 1975, **8**, 139.

² C. Paal, *Ber.*, 1885, **18**, 2255.

³ M. Cinquini, S. Colonna, and R. Giovini, *Chem. and Ind.*, 1969, 1737.

⁴ L. E. Saris and M. P. Cava, *J. Amer. Chem. Soc.*, 1976, **98**, 867.

⁵ J. Stackhouse, G. H. Senkler, Jr., B. E. Maryanoff, and K. Mislow, *J. Amer. Chem. Soc.*, 1974, **96**, 7836.

Paper J

Nonclassical Selenoloselenophenes and Selenolothiophenes.

Nonclassical Selenoloselenophenes and Selenolothiophenes

Andreas Konar and Salo Gronowitz

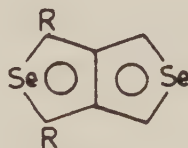
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ABSTRACT

Several synthetic approaches to the nonclassical selenoloselenophenes 2, 3, 4, and selenolothiophenes 84, 86, 87, 95 and 96 have been tried. Acid- and base-catalyzed dehydration of selenoxides or sulfoxides, base-catalyzed reductive debromination of selenium dibromides, reaction of suitable dibenzyl-substituted compounds with sulfur, reaction of dibenzoyl- and tetrabenzoyl-substituted compounds with phosphorus pentasulfide or pentaselenide, and base-catalyzed rearrangement of thieno- and selenolo-fused 1,2-dithianes all have been used, although most of them with no success. Decomposition of selenoxides and sulfoxides by acid and selenium dibromides by base were the only methods leading to the nonclassical systems. The first of them, used originally by Cava and his coworkers in their preparations of thieno[3,4-c]thiophene derivatives, still seems to be a method of choice. In some cases, the NMR and UV spectra of the unstable selenoloselenophene and selenolothiophene derivatives were recorded. These spectra, together with the formation of 1,3-adducts with some dienophiles, were taken as an evidence for the transient existence of the above-mentioned systems.

INTRODUCTION

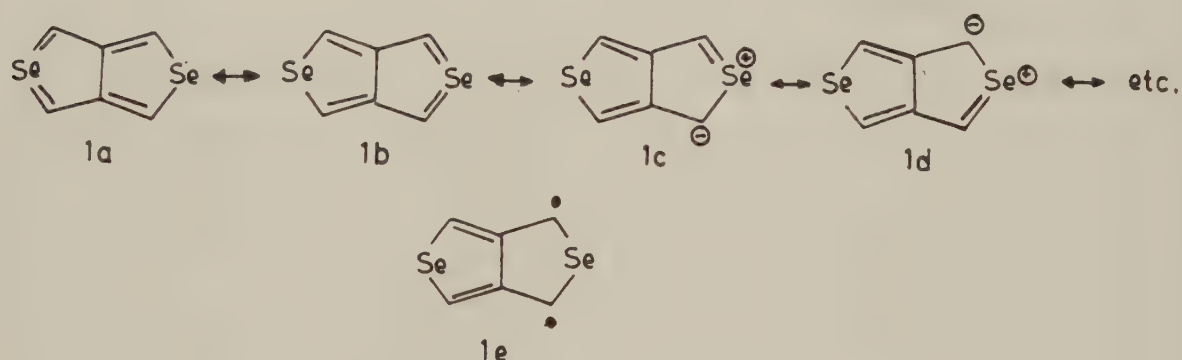
Some years ago, in a preliminary communication,¹ we had reported some results concerning syntheses of 1,3-dimethyl- and 1,3-dicarb-ethoxyselenolo[3,4-c]selenophenes (2) and (3), the first derivatives of the nonclassical selenolo[3,4-c]selenophene system (1). It is the purpose of this paper to give the detailed description of this work, as well as of the synthesis of the 1,3-diphenyl-substituted derivative 4, and some mixed sulfur-selenium systems. Different approaches to these disubstituted and also some tetrasubstituted derivatives will be described.



- 1 R=H
- 2 R=CH₃
- 3 R=CO₂C₂H₅
- 4 R= Ph

The term "nonclassical" has been used by Cava et al.² in relation to the possibility that, in some sulfur-containing species, the participation of d-orbitals may be important in the bonding. Bicyclic 10 π -electron heterocycles containing a "nonclassical" thiophene nucleus constitute a good example of such species and are thus of considerable theoretical interest. Reviews dealing with this topic include "Nonclassical Condensed Thiophenes" by Cava and Lakshmikantham,² "Heteropentalenes" by Potts,³ and "Mesomeric Betaine Derivatives of Heteropentalenes" by Ramsden.⁴ A brief look at these

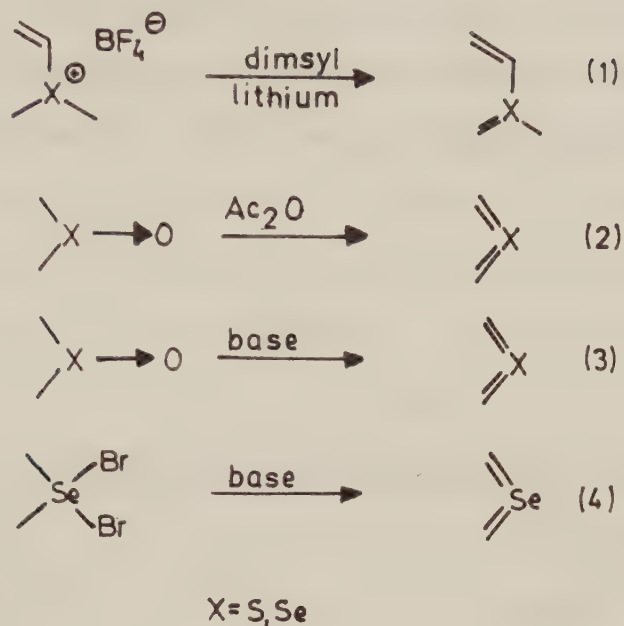
titles reveals that even the nomenclature of this class of compounds is still the subject of discussion. In this paper, we intend to use the term "nonclassical" in regard to the selenolo[3,4-c]selenophene system (1) in the sense, that the only uncharged resonance contributors, which can be written must contain a tetravalent selenium atom in one of the rings, as in structure 1a or 1b. The symmetry of the system would appear to make it a particularly favourable molecule for d-orbital participation, in the absence of which the molecule must either have a character of a selenium ylide, as in structures 1c, 1d etc., or of a diradical, as in structure 1e.



On the other hand, as pointed out by Ramsden,⁴ "there is no law of nature which requires that molecules be represented by purely covalent structures. The observation that without inclusion of d-orbitals the thieno[3,4-c]thiophenes can only be represented as mesomeric betaines (i.e. in our case as selenium ylides 1c, 1d etc.) is not sufficient justification, without other evidence, for invoking d-orbital participation".

There are few reported synthetic routes leading to a nonclassical sulfur or selenium heterocycle and the most important of them are

summarized in Scheme 1.



Scheme 1

Route (1) utilizes the treatment of thia- or selenatetrafluoroborates with dimsyl lithium in a mixture of toluene and dimethoxyethane, as reported by Mislow *et al.* in their preparations of thia-⁵ and selenabenzenes.⁶ It is, however, not applicable for the synthesis of nonclassical thiophenes or selenophenes, for which the most useful approach is that of route (2), namely the Pummerer-type dehydration of a suitable sulfoxide or selenoxide, as proposed by Cava *et al.* (cf. Ref. 2 and references therein). Formation of some condensed thiophenes by a base-catalyzed sulfoxide dehydration, according to route (3) in Scheme 1, was also reported by Cava *et al.*,⁷ as well as the base-catalyzed reductive debromination of a selenium dibromide,⁸ according to route (4).

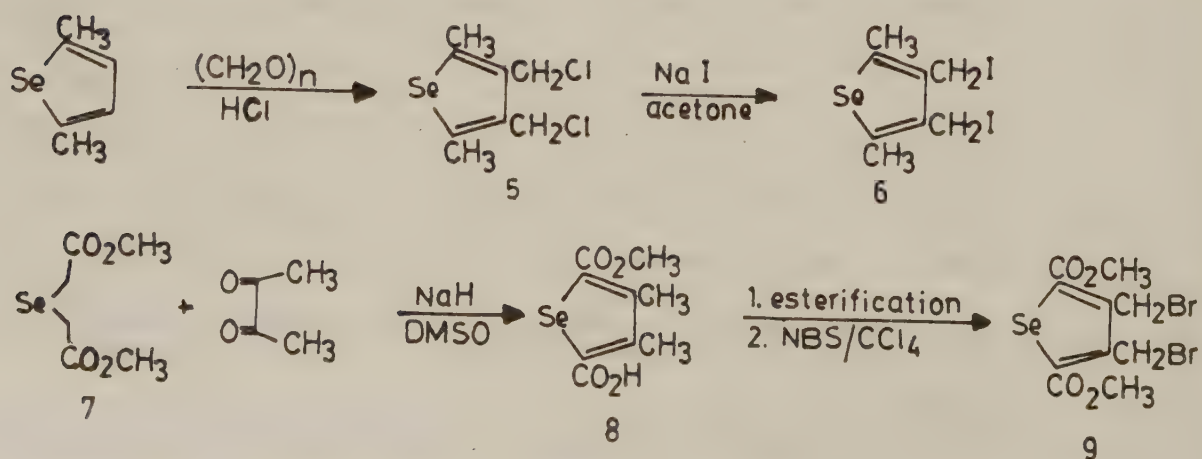
In our efforts to prepare the nonclassical selenolo[3,4-c]-selenophene system (1), we have made use of all the methods outlined

in Scheme 1, with the exception of the first which is not directly applicable. There are still some other, probably less general, approaches to a nonclassical sulfur or selenium heterocycle, and these will be discussed in connection with the particular reactions.

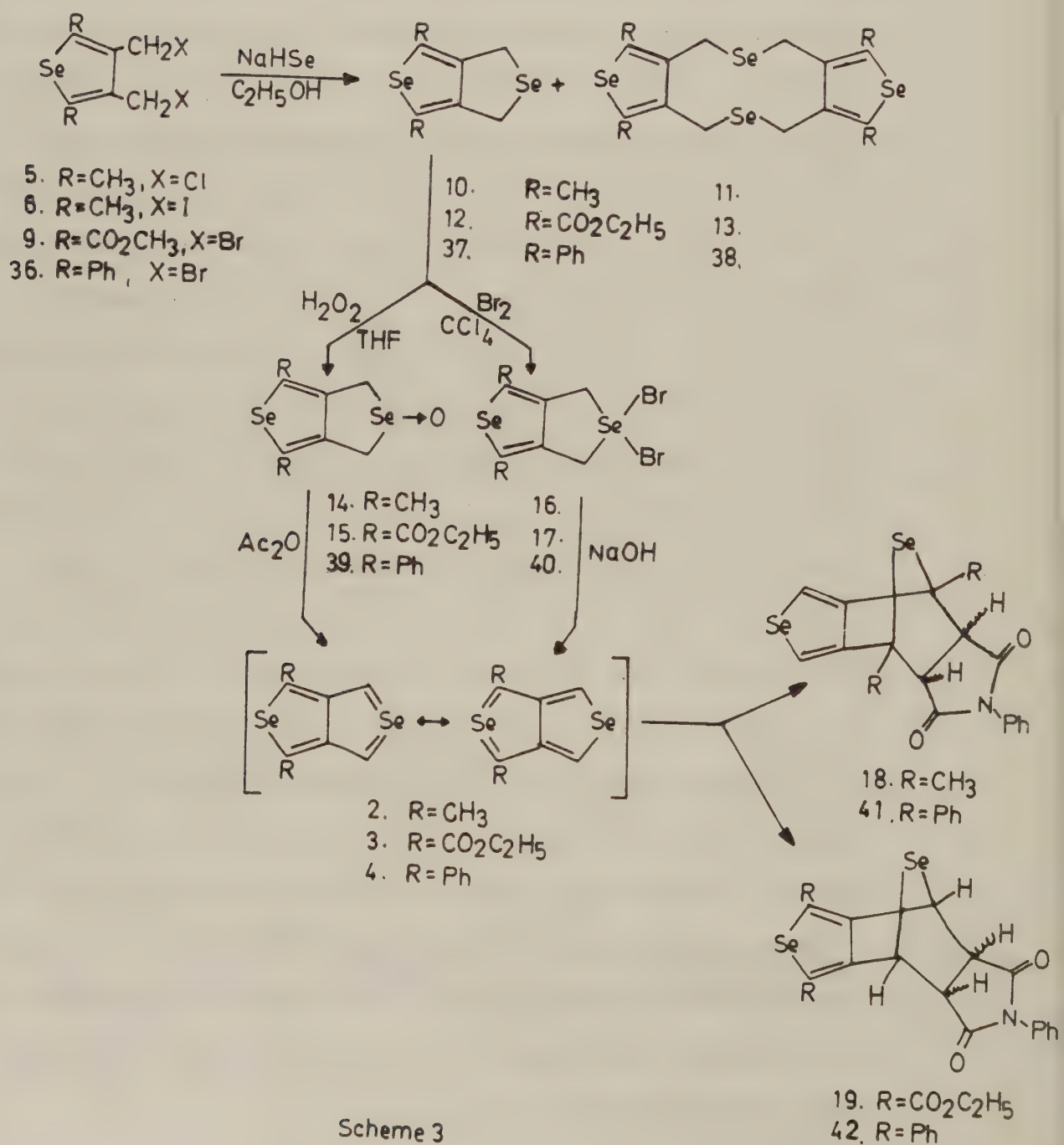
RESULTS

1,3-Dimethyl- and 1,3-Dicarbethoxyselenolo[3,4-c]selenophenes

The dimethyl- and dicarbomethoxy derivatives of thieno[3,4-c]-thiophene, reported by Cava *et al.*,² were synthesized by dehydration of the corresponding sulfoxides, for which reason an analogous synthetic approach to 2 and 3 was chosen. The synthesis of benzo[c]selenophene by dehydrobromination of the corresponding selenium dibromide,⁸ has also prompted us to follow this synthetic route. Both approaches are outlined in Scheme 3, where 3,4-bishalomethylselenophenes 5 and 9 were used as starting materials. Their syntheses are shown in Scheme 2.



2,5-Dimethylselenophene was prepared from 2,5-hexanedione and phosphorus pentaselenide⁹ or from selenophene via consecutive metalation and treatment with dimethyl sulfate. Chloromethylation of 2,5-dimethylselenophene with paraformaldehyde and hydrogen chloride in acetic acid afforded 3,4-bischloromethyl-2,5-dimethylselenophene (5) in 89 % yield. Preparation of the dicarbomethoxy-substituted selenophene 9 was a three-step synthesis, the first step of which was a Hinsberg reaction of dimethyl selenodiacetate (7) and diacetyl, in analogy to the procedure described for the sulfur analog of 8.¹⁰ Preparation of 7 in one step from aqueous sodium hydrogen selenide¹¹ and methyl chloroacetate appeared to be a better procedure than that described by Backer and Stevens.¹² Esterification and subsequent NBS bromination of the half-acid 8 gave the desired selenophene 9 in 37 % over-all yield. The ring-closure reactions of 5 and 9 with ethanolic sodium hydrogen selenide gave mixtures of the required dihydroselenophenes 10 or 12, their dimers 11 or 13, and even higher oligomers, from which the monomers could be separated by steam distillation (10 in 45 % yield) or fractional crystallization (12 in 88 % yield). This difference in yields of the ring-closed products 10 and 12 was attributed partly to the better leaving-group character of the bromine atoms in 9 than of the chlorine atoms in 5. For this reason, we have synthesized the bisiodomethyl derivative 6 which, however, on ring-closure with NaHSe gave the comparable yield of the dihydroselenophene 10. Although the cyclizations with the ethanolic NaHSe solution were carried out at room temperature, transesterification of the dimethyl ester 9 occurred quantitatively, only the diethyl ester 12 being isolated.



Scheme 3

All attempts to purify the selenoxide 14 resulted in decomposition accompanied by a development of an intense, red-pink, fluorescent colour of the solution. When a solution of 14 in acetic anhydride was heated to reflux under nitrogen, an intense red-violet, fluorescent colour developed rapidly. This colour, which we attribute to the selenoloselenophene 2, remained unchanged after an additional 3 hours of refluxing. We could not, however, isolate this violet product, owing to its sensitivity to air. Oxidation of 12 with sodium metaperiodate in methanol-water¹³ did not allow isolation of the selenoxide 15 in the pure state, as the extraction with any water-immiscible organic solvent gave the deep violet fluorescence of the organic phase extracts. Oxidation with hydrogen peroxide in THF led directly to the development of this violet colour, which we attribute to the selenoloselenophene 3. Upon attempted isolation of these violet products, mixtures of selenides 10 or 12, their dimers 11 or 13 and higher oligomers were obtained in both cases.

Extraction of the methanol-water solution of the selenoxide 15 with *n*-hexane allowed, however, recording of a UV spectrum of the violet product, which showed $\lambda_{\text{max}} = 563 \text{ nm}$. Extraction with hexadeuteriobenzene made possible recording of the NMR spectrum, which besides the carbethoxy groups, showed a single peak for the aromatic protons at δ 10.04 ppm. This peak disappeared within 0.5 hour, during which time the original violet colour of the solution faded.

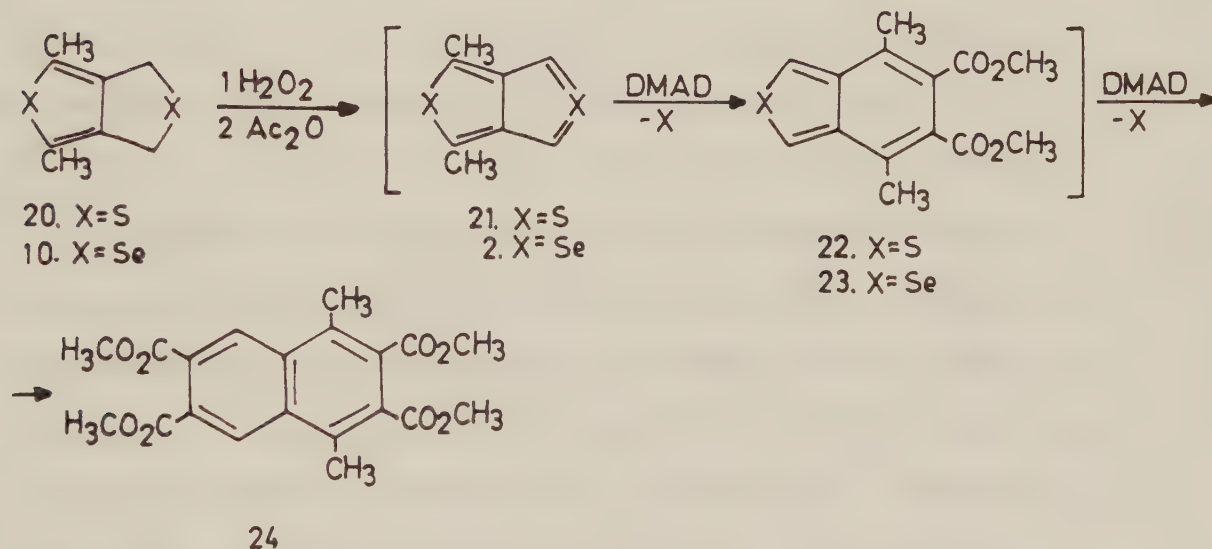
The dibromides 16 and 17 were decomposed within a few minutes when stirred with 40 % sodium hydroxide solution at 0°C under nitrogen. When the resulting milky emulsions were stirred with *n*-hexane, 2 and 3 respectively, were slowly released into the organic phase. This process

was much faster when benzene was used and could be followed by the appearance of a deep violet colour remaining for over 2 hours in the case of 2 and for over 5 hours with 3, which might indicate that the derivatives of the selenolo[3,4-c]selenophene system (1) substituted by the electron-withdrawing groups are more stable than those substituted by electron-donating ones.

As mentioned above, selenoloselenophenes 2 and 3 are too unstable to be isolated in the pure state, but they can be trapped with various dipolarophiles in 1,3-dipolar cycloaddition reactions. As pointed out by Ramsden,⁴ such reactions are mainly governed by two factors: (i) the energy and symmetry of the HOMO of the heteropentalene and (ii) the thermodynamic stability of the cycloadduct. In the case of nonclassical condensed thiophenes,² dienophile addition takes place at the ring of highest electron density, i.e. as expected for an aromatic, delocalized system. If the dehydration of selenoxides 14 and 15 was carried out in the presence of N-phenylmaleimide (NPM) or if NPM was added to the violet solutions of 2 or 3, the reactions were normally completed within a few minutes, as indicated by the disappearance of the violet colour. In both cases we were able to isolate a few crystals of the adducts, the composition of which were confirmed by their mass spectra. Unfortunately, we were not able to record their NMR spectra, for which reason the structure assignments are, as yet, uncertain as to the site of dienophile addition, as well as to the endo/exo conformation of the adducts. Most probably, reaction with NPM takes the same course for 2 and 3 as for the corresponding sulfur analogs,² i.e. the addition takes place at the ring of highest electron density and both endo and exo adducts are generated with the exo conformation predominating.

In Scheme 3, the conformations are not specified, but the anticipated sites of addition are pointed out by only drawing structure 18 for the NPM adduct of the dimethyl-substituted selenoloselenophene 2 and structure 19 for the dicarbethoxy-substituted selenoloselenophene 3. Further efforts to confirm the proposed structures 18 and 19 will be made.

N-phenylmaleimide was the dienophile reagent most often used by Cava et al.² in order to trap the nonclassical thienothiophene derivatives, but the use of many other dienophiles is, of course, also possible. Some results obtained with dimethyl acetylenedicarboxylate (DMAD) are shown in Scheme 4.

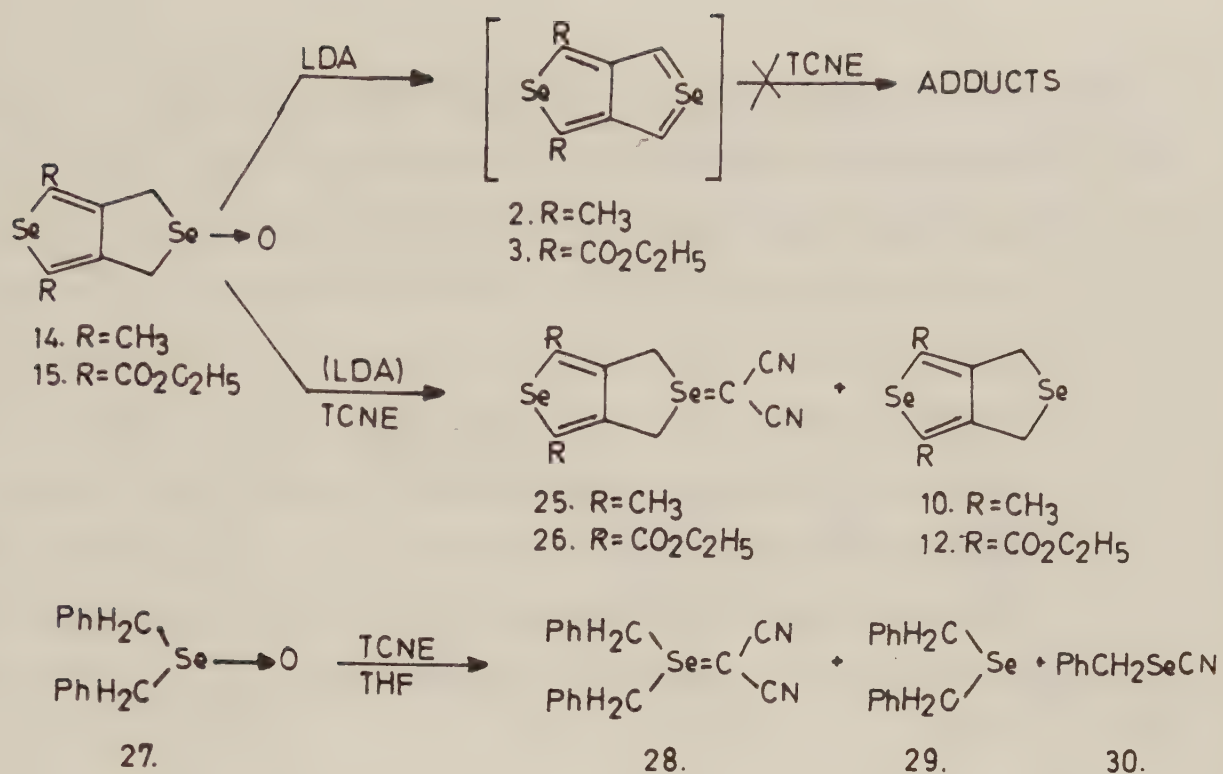


Scheme 4

When the excess of DMAD was used, the known¹⁴ tetracarboxymethoxy naphthalene 24, along with some polymeric products, was the only isolable product, both on trapping of the selenophene 2 or thiophene 21. These spontaneous extrusions of sulfur or selenium from the

primarily formed, bridged adducts were not eliminated by using equimolar amounts of DMAD, 24 still being the product of both reactions. Not even the aromatized adducts 22 or 23 were observed, indicating the facile dienophile addition of these, benzo[c]thiophene 22 and benzo[c]selenophene 23, systems.

Cava *et al.*⁷ have recently reported the formation of some condensed thiophenes by base-catalyzed dehydration of sulfoxides (*cf.* route 3 of Scheme 1), employing such bases as different Grignard reagents, methyl lithium, sodium hydroxide or lithium diisopropylamide (LDA), with the latter giving the highest yields. When the LDA-dehydration of the selenoxide 14 was attempted, the intensified violet colour of the originally colourless solution developed and vanished within a few seconds. The selenide 10 along with some polymeric materials were the only isolable products. Attempts to trap selenoloselenophene 2, which may have formed, with NPM or DMAD were not successful. If, however, tetracyanoethylene (TCNE) was used as dienophile, the reaction products turned out to be the selenonium dicyanomethylides 25 or 26 along with small amounts of the selenides 10 or 12. Very recently, a similar reaction of dibenzyl selenoxide (27) with TCNE has been reported¹⁵ (*cf.* Scheme 5), which renders the question whether lithium diisopropylamide really brought about the formation of selenoloselenophenes 2 and 3. In the control experiment, the selenoxide 14 was therefore reacted with TCNE, indeed giving the ylide 25, as indicated in Scheme 5.



Scheme 5

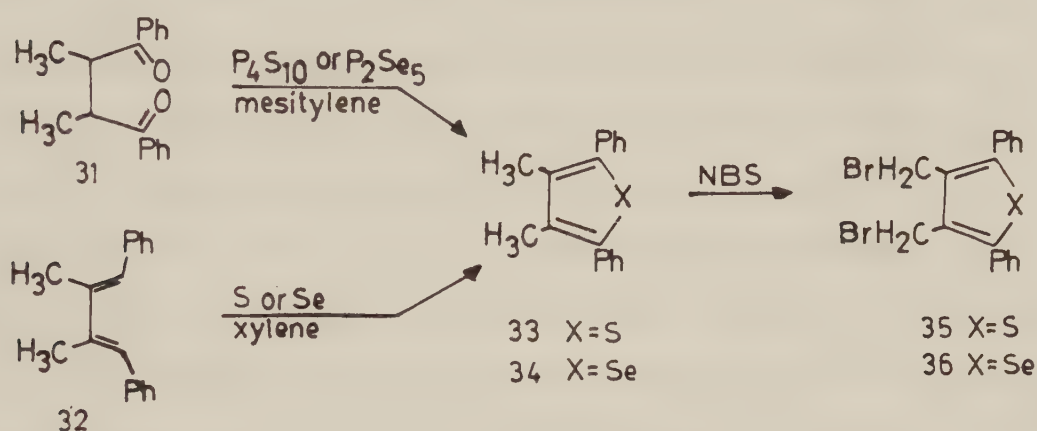
Although benzyl selenocyanate (30) was the main product of the reaction of dibenzylselenoxide (27) with TCNE,¹⁵ no selenocyanates could be detected among the products of the reaction of 14 shown in Scheme 5. Failure to obtain the adducts of 2 or 3 with TCNE in the above reaction might indicate that selenophenes 2 and 3, if formed, immediately decompose in the presence of such strong base as LDA or that TCNE is not a sufficiently reactive dienophile to bring about the cycloaddition reactions with 2 and 3. Since trapping experiments with both NPM, DMAD and 4-phenyl-1,2,4-triazoline-3,5-dione (cf. below) in the presence of LDA have also failed, the former explanation is then more probable.

In view of the considerable difficulties encountered in trapping the selenoloselenophenes 2 and 3 as their Diels-Alder adducts, we have also tried to use 4-phenyl-1,2,4-triazoline-3,5-dione, which is known to undergo a Diels-Alder reaction with most dienes and is, in fact, the most reactive dienophile so far reported (10^3 times more reactive than TCNE and 2×10^3 times more reactive than maleic anhydride),^{16,17} There are several ways of preparing this dione; we have found the recently reported oxidation of 4-phenyl urazole with N-bromosuccinimide,¹⁸ the most convenient. Unfortunately, neither this approach turned out to be successful and no adducts of the dione with 2 or 3 could be isolated.

1,3-Diphenyl- and 1,3,4,6-Tetraphenyl-Substituted Selenolo[3,4-c]-selenophenes and Selenolo[3,4-c]thiophenes

The first and to date, the only stable derivative of the non-classical thieno[3,4-c]thiophene was tetraphenylthieno[3,4-c]thiophene (55) reported in 1969 by Cava et al.² Our efforts to prepare the corresponding tetraphenylselenolo[3,4-c]selenophene were described in an earlier publication.⁹ Here the synthetic approaches to some other, phenyl-substituted systems will be described. It was hoped that the stabilizing effect of the phenyl groups, such as in tetraphenylthieno[3,4-c]thiophene (55), will also be operative in the disubstituted system 4, making it more stable than selenoloselenophenes 2 or 3. In view of the recent results concerning electronic structure of 55,^{19,20} where the steric interference by the 1,3-phenyl substituents was found to be the main factor responsible for the stability of the thieno-thiophene 55, it became however, doubtful if the presence of only two phenyl groups in 4 will be sufficient to stabilize the system more than the presence of the two electron-withdrawing carbethoxy groups in 3.

The required starting material for the synthesis of 4 was again a 3,4-bishalomethyl selenophene 36 or for the selenolothiophene system - a thiophene 35. Their syntheses are outlined in Scheme 6, where two different routes are shown.



Scheme 6

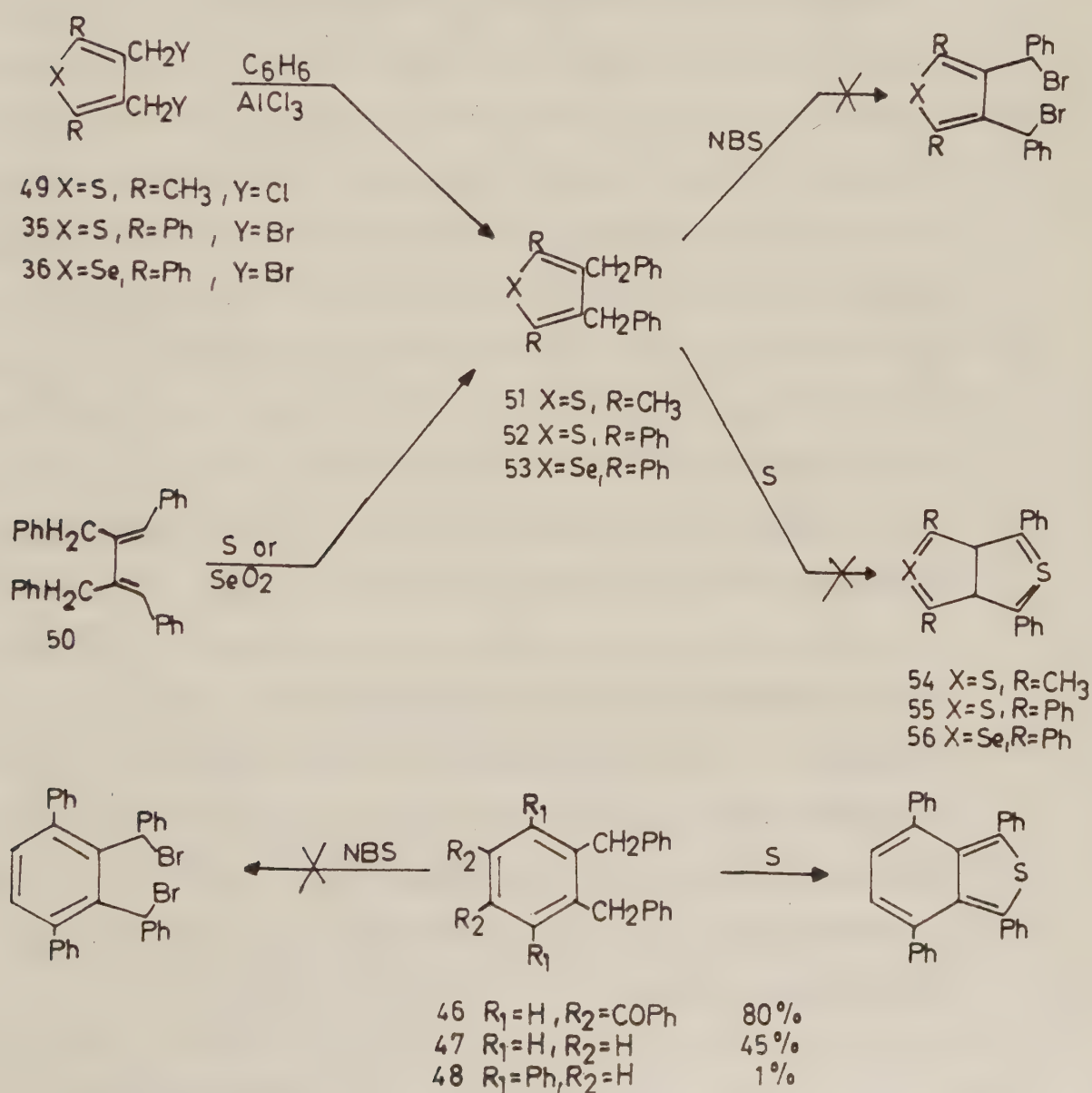
3,4-Dimethyl-2,5-diphenylthiophene (33) or -selenophene (34) were first prepared by Wakatsuki *et al.*²¹ in the reaction of cobaltocyclopentadiene complex with sulfur or selenium, respectively. We have later prepared 33 and 34 by reacting 2,3-dimethyl-1,4-diphenyl-1,4-butanedione (31) with phosphorus pentasulfide or pentaselenide,⁹ as outlined in Scheme 6. Both reactions gave ca. 50 % yield of 33 or 34. An equally efficient way to these compounds, which moreover does not involve preparation and handling of the sensitive phosphorus pentaselenide reagent,⁹ is the reaction of 2,3-dimethyl-1,4-diphenyl-1,3-butadiene (32) with elemental sulfur or selenium. Action of sulfur on 1,3-dienes is an old approach to substituted thiophenes²² and the particular reaction of butadiene 32 with sulfur to give 33 has, in fact, been reported quite recently.²³ Preparation of selenophenes from conjugated dienes and elemental

selenium has also been described by several workers,²⁴ although it was not used for the selenophene 34. NBS bromination of 33 and 34 afforded the desired bisbromomethyl derivatives 35 and 36 in good yields. Ring-closure of the selenophene 36 with ethanolic sodium hydrogen selenide gave a mixture of the dihydroselenophene 37, its dimer 38 and even higher oligomers, from which the monomeric 37 was separated by fractional crystallization. Oxidation of 37 gave the selenoxide 39 and bromination afforded the selenium dibromide 40 in good yields. All of the above-mentioned transformations of 36 are illustrated in Scheme 3, where R = Ph. Similar reactions were also carried out with thiophene 35 giving the ring-closed dihydroselenolothiophene 43, the selenoxide 44 and the selenium dibromide 45, with the structures analogous to 37, 39 and 40, respectively, as shown in Scheme 10.

When a solution of the selenoxide 39 in acetic anhydride was heated to reflux under nitrogen, an intense red-violet colour developed rapidly. This colour, which we attribute to the selenoloselenophene 4, remained unchanged after an additional 4 hours of refluxing. The dibromide 40 was decomposed within a few minutes when stirred with 40 % sodium hydroxide solution at 0°C under nitrogen. When the resulting milky emulsion was stirred with benzene, 4 was released into the organic phase, as indicated by appearance of the intense fluorescent, red-pink colour of the benzene solution. When a solution of NPM in benzene was added, the red colour disappeared rapidly and a few crystals of the NPM-adduct precipitated. Its composition was confirmed by the mass spectrum but unfortunately, we were not able to record the NMR spectrum in order to establish the site of the dienophile addition. In Scheme 3, both the structures 41 and 42 are therefore depicted. Similar results

were obtained with the sulfur analogs of the above-mentioned compounds: the selenoxide 44 and the dibromide 45. Again, the structures of the NPM-adducts formed could only be confirmed by their mass spectra.

Very recently, Lepage *et al.*²⁵ have observed the formation of benzo[c]thiophene derivatives on treatment of some *o*-dibenzylbenzenes with sulfur. Especially a very good yield of the reaction of compound 46 (cf. Scheme 7), has prompted us to follow this synthetic approach to tetraphenyl derivatives 55 and 56.



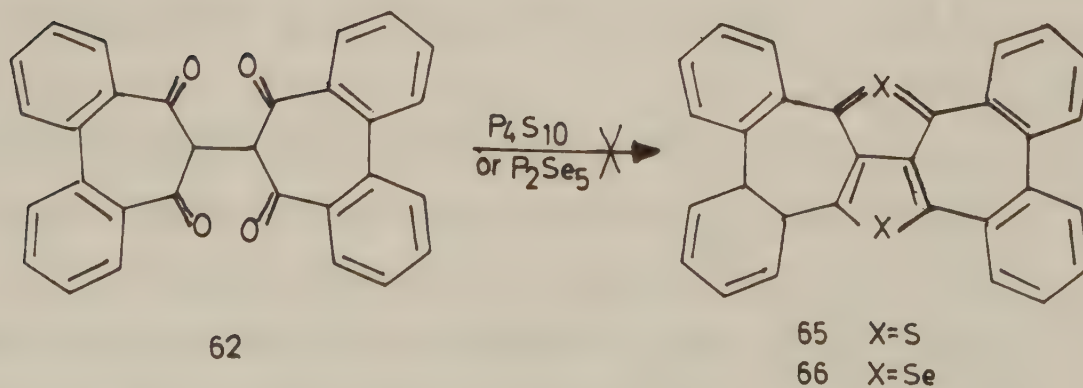
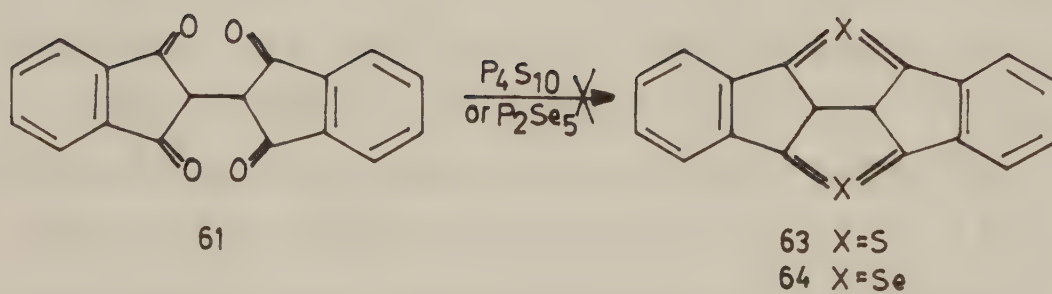
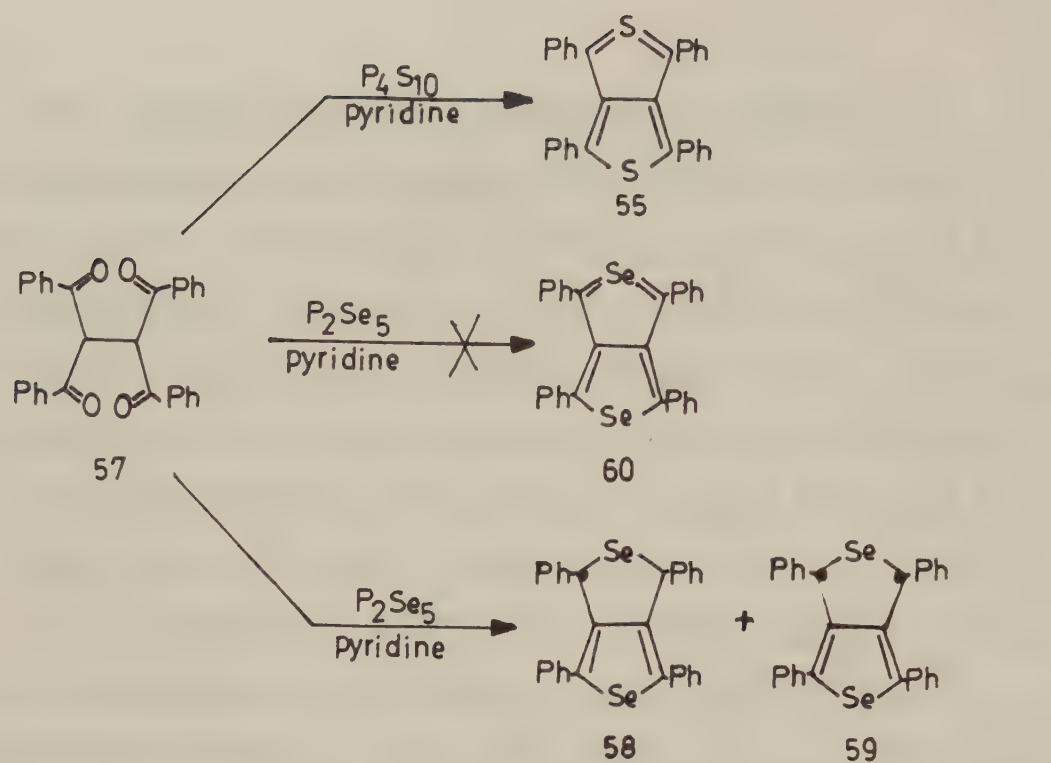
Scheme 7

The required 3,4-dibenzyl-substituted compounds 52 and 53, have been synthesized by Lepage et al.²⁵ by action of sulfur or selenium dioxide on the butadiene 50; the thiophene 52 in 85 % and the selenophene 53 in 13 % yield. Since we had access to the bisbromo-methyl compounds 35 and 36, we have instead utilized the Friedel-Crafts alkylation with benzene, which afforded the dibenzyl compounds in ca. 55 % yield, as illustrated in Scheme 7. Reaction of 52 and 53 with sulfur at 300°C did not, however, afford the nonclassical tetraphenyl-thieno[3,4-c]thiophene (55) or selenolothiophene 56. This could be due to the instability of 55 and 56 under the reaction conditions, although at least 55, melting at 257-258°C without decomposition,² could be expected to survive the high temperature of the reaction. Another reason for this failure might be the same one which caused the low yield of the reaction of the terphenyl 48, where the main product turned out to be not the benzo[c]thiophene but rather an indenofluorene, i.e. a product of the carbocyclization reaction. In fact, mass spectrographic analysis of the product mixture from the reaction of 52 with sulfur, indicated the presence of the corresponding carbocyclization product, 10,11-diphenyl-diindeno[1,2-b:2',1'-d]thiophene, (m/e 412, C₃₀H₂₀S). In order to avoid the possibility of such a reaction, we have carried out the reaction of the dimethyl-substituted thiophene 51²⁶ with sulfur at 300°C, but neither in this case the formation of thienothiophene 54 could be observed. Reactions of the 3,4-dibenzyl compounds 51-53 with sulfur were also carried out in the presence of NPM in order to trap the compounds 54-56, if they would form, but no dienophile addition products were detected.

Still another way to utilize the compounds 51-53 for the synthesis of the nonclassical 54-56, could have been bromination in the benzylic positions, subsequent cyclization with sodium sulfide or selenide and the usual interconversions into the nonclassical systems. This route failed, however, already in the first step since NBS bromination of 51 gave the product brominated at the methyl groups and not in the benzylic positions, while bromination of both 52 and 53 failed to occur. This is possibly not surprising in view of the similar failure to brominate the dibenzyl *p*-terphenyl 48.²⁵

Tetraphenylthieno[3,4-*c*]thiophene (55) has been prepared by Cava *et al.*^{2,27} in one step in 96 % yield by reacting tetrabenzoylthane (57) with phosphorus pentasulfide in pyridine. Similar reaction of 57 with phosphorus pentaselenide in pyridine led only to a mixture of *trans*- and *cis*-dihydroselenophenes 58 and 59, but no tetraphenyl-selenolo[3,4-*c*]selenophene (60) could be detected.⁹ In order to further investigate this double-sided ring-closure of the tetraone skeleton and at the same time additionally increase the possibility for delocalization in the projected system, we have attempted the P_4S_{10} and P_2Se_5 ring-closure of the tetraketones 61 and 62, as shown in Scheme 8.

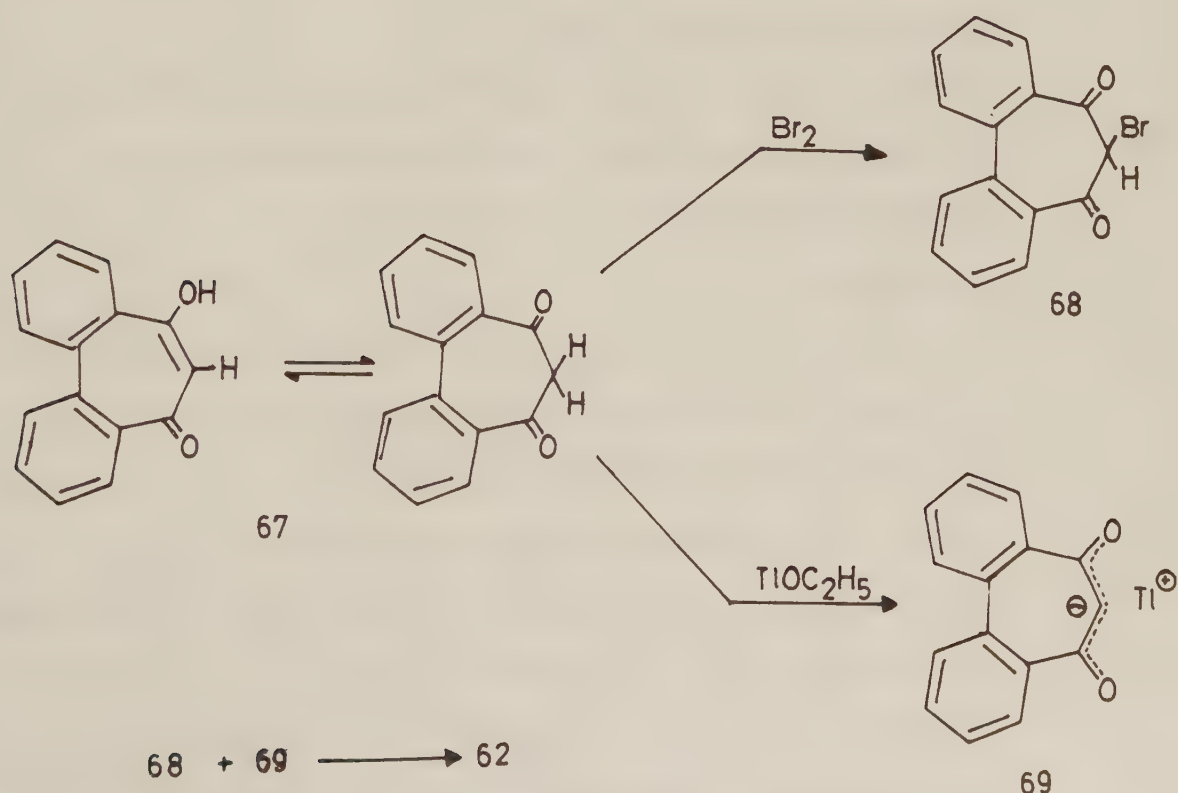
As could be expected, the reaction of the readily available bisindandione 61²⁸ with phosphorus pentasulfide or -selenide did not afford compounds 63 and 64 with their highly strained structures containing four fused five-membered rings. Expansion of the 5-membered rings connected to the tetraketone frame in 61 into 6-membered rings would give a compound formally derived by joining two phenalene-1,3-dione moieties. Inspection of the molecular models revealed, that also such a compound would suffer from considerable strain and would not be planar.



Scheme 8

Another expansion into 7-membered rings would give compound 62, the models of which looked more promising in regard to coplanarity and lack of strain.

The most straight-forward synthesis of 62 includes a coupling of two molecules of the known²⁹ dibenzocycloheptadienone 67, preferably via monoalkylation at carbon with its own monohalo derivative. Although excess of bromine gives the dibromo derivative of 67 even at room temperature, we have found that equimolar amounts of bromine at 12°C give the required monobromo compound 68 in good yield. Traces of a ring-contracted product, phenantro-quinone, were also detected. Monoalkylation at carbon of β -dicarbonyl anions is often accompanied by side-reactions like dialkylation, O-alkylation, β -keto cleavage, oxidative coupling, Claisen condensations, etc. By using a thallium(I) salt of the β -dicarbonyl compound, all of the above-mentioned competitive reactions can be avoided.³⁰ Indeed, heating of the easily prepared thallium(I) salt 69 with a suspension of the monobromo cycloheptenedione 68 in ligroin, afforded the required tetraketone 62 in 74 % yield (cf. Scheme 9). Unfortunately, neither ring-closure with P_4S_{10} nor with P_2Se_5 gave the expected products 65 and 66.



Scheme 9

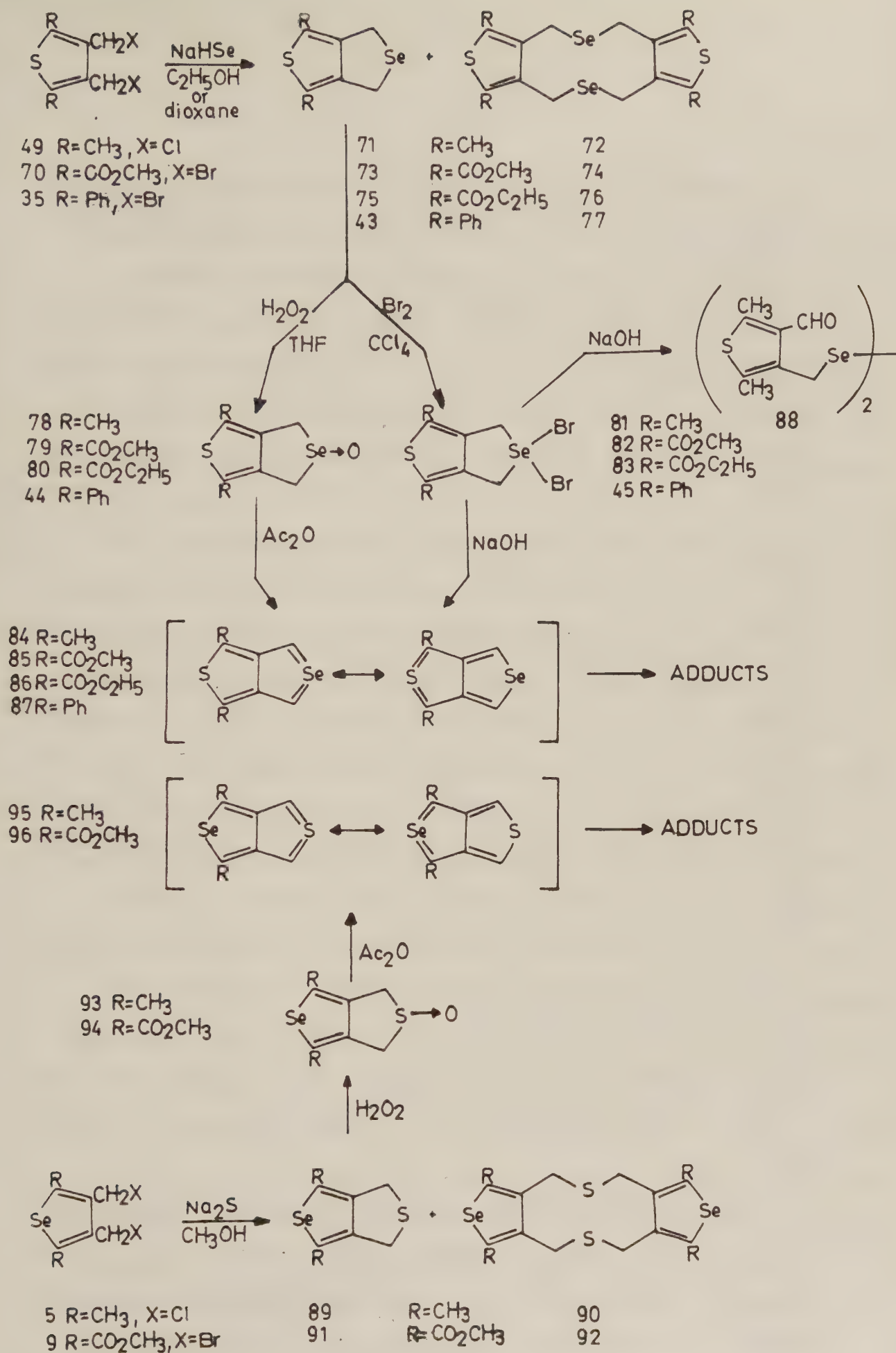
1,3- or 4,6-Disubstituted Selenolo[3,4-c]thiophenes

As mentioned in the preceding section, the reaction sequence carried out on 3,4-bisbromomethyl-2,5-diphenylselenophene (36) leading to 1,3-diphenylselenolo[3,4-c]selenophene (4) (cf. Scheme 3), was also applied to the corresponding thiophene 35 with the objective of synthesizing the nonclassical selenolothiophene 87 (cf. Scheme 10). We have also used the same approach, i.e. the NaHSe ring-closure of 3,4-bishalomethylthiophenes, for the preparation of the dimethyl and dicarbethoxy derivatives 84 and 86. In this section, we describe the attempts to synthesize derivatives of the nonclassical selenolo[3,4-c]thiophene system along two different routes:

- (i) the above-mentioned ring-closure of 3,4-bishalomethylthiophenes with sodium hydrogen selenide or
- (ii) the ring-closure of 3,4-bishalomethylselenophenes with sodium sulfide both followed by oxidation and dehydration of the selenoxides, respectively sulfoxides formed.

In the first approach, the selenides obtained after NaHSe ring-closure, can also be brominated and the selenium dibromides reduced to a selenolo[3,4-c]thiophene derivative. Both routes are briefly outlined in Scheme 10.

The ring-closure reactions of the known bishalomethylthiophenes 49³¹ and 70³² with ethanolic sodium hydrogen selenide afforded mixtures of the required dihydroselenolothiophenes 71 and 75, their dimers 72 and 76, and even higher oligomers, from which the monomers could be separated by steam distillation (71 in 50 % yield) or fractional crystallization (75 in 68 % yield). Similarly to the cyclization of the selenophene 9, also the cyclization of the thiophene 70 was accompanied by a quantitative transesterification, only the diethyl ester 75 being isolated.



Scheme 10

Hydrogen peroxide oxidation of 71 and 75 gave the dimethyl- and dicarbethoxy-substituted selenoxides 78 and 80, respectively, and bromination with bromine in carbon tetrachloride afforded the corresponding selenium dibromides 81 and 83 in very good yields. Only the selenoxide 78 could be isolated in the pure state, since oxidation of 75 led, similarly to the oxidation of its selenium analog 12, to the development of an intense, red-pink colour of the solution. This colour, which we attribute to the selenolothiophene 86, remained unchanged for more than 3 hours under nitrogen and corresponded to a band of $\lambda_{\text{max}} = 538 \text{ nm}$ in hexane. Upon attempted isolation of this red-pink product, a mixture of 75, 76 and some polymeric materials was obtained. The dimethyl-substituted selenoxide 78, although stable for a few days at room temperature, could not be purified by recrystallization, all attempts leading to a development of a pink colour of the solution. When an NMR spectrum of 78 in CDCl_3 was recorded, the expected singlets of the methylene and methyl protons could be observed at δ 3.94 and 2.27 ppm, respectively. If, however, the spectrum was recorded in a DMSO-d_6 solution, the intensity of the initially observed signals at δ 4.27 and 2.34 rapidly decreased and two new singlets at δ 10.04 and 2.68, indicating formation of the nonclassical selenolothiophene 84, appeared. This was accompanied by a slight coloration of the solution and, within an hour, followed by disappearance of the new signals as the pink colour faded.

When a solution of the selenoxide 78 in acetic anhydride was heated to reflux under nitrogen, an intense red-pink colour developed rapidly. This colour, which we attribute to the selenolothiophene 84, remained unchanged for only one hour of refluxing. We could not isolate this

coloured product owing to its sensitivity to air, but in a similar dehydration in the presence of equimolar amounts of *N*-phenylmaleimide, we were able to trap the selenolothiophene 84 as its 1,3-adduct. NMR spectrum of this adduct indicated addition of the dienophile only at the alkyl-bearing thiophene ring, as was also the case with the corresponding thienothiophene 21.² Attempts to trap 84 with dimethyl acetylenedicarboxylate led directly to the tetracarbomethoxy naphthalene 24 (cf. Scheme 4).

As mentioned above, the dicarbethoxy-substituted selenoxide 80 could not be isolated in the pure state, since it decomposed to the nonclassical selenolothiophene 86. Unfortunately, our attempts to trap 86 with *N*-phenylmaleimide failed, the only isolable products being the selenide 75 and its dimer 76. Isolation and structure determination of the primary NPM-adduct of 86 would confirm if the addition took place at the sites of highest electron density, *i.e.* in the selenophene ring of 86. Trapping experiments with tetracyanoethylene brought about the formation of 1,3-dicarbethoxy-4H,6H-selenolo[3,4-*c*]thiophene-5-dicyanomethylide with the structure analogous to that of 26 (cf. Scheme 5).

During the time this work was in progress, Saris and Cava³³ reported generation and trapping of 1,3-dimethyl- and 1,3-dicarbomethoxyselenolo-[3,4-*c*]thiophenes (84) and (85), respectively. The synthetic approach used by them followed that outlined in the upper half of Scheme 10, with the exception that ring-closure reactions of 49 and 70 were brought about by aqueous sodium hydrogen selenide in dioxane, for which reason no transesterification of 70 to give the diethyl ester 75 was observed. The monomers 71 and 73 were separated from their dimers by sublimation and, in contrast to 80, the dicarbomethoxy-substituted selenoxide 79

was reported to be stable. The spectral data of the NPM-adduct of 84 were in accord with those observed by us, but no NPM-adduct of 85 was reported. However, the trapping of 85 with DMAD afforded 1,3,5,6-tetracarbomethoxybenzo[c]thiophene, formed by aromatization of the primary NPM-adduct by loss of the selenium atom from the bridge. This confirms that the addition of DMAD to 85 took place at the ring of the highest electron density. The UV spectrum of 85 in ethanol showed $\lambda_{\text{max}} = 536 \text{ nm}$, as compared to 538 nm for 86 in hexane.

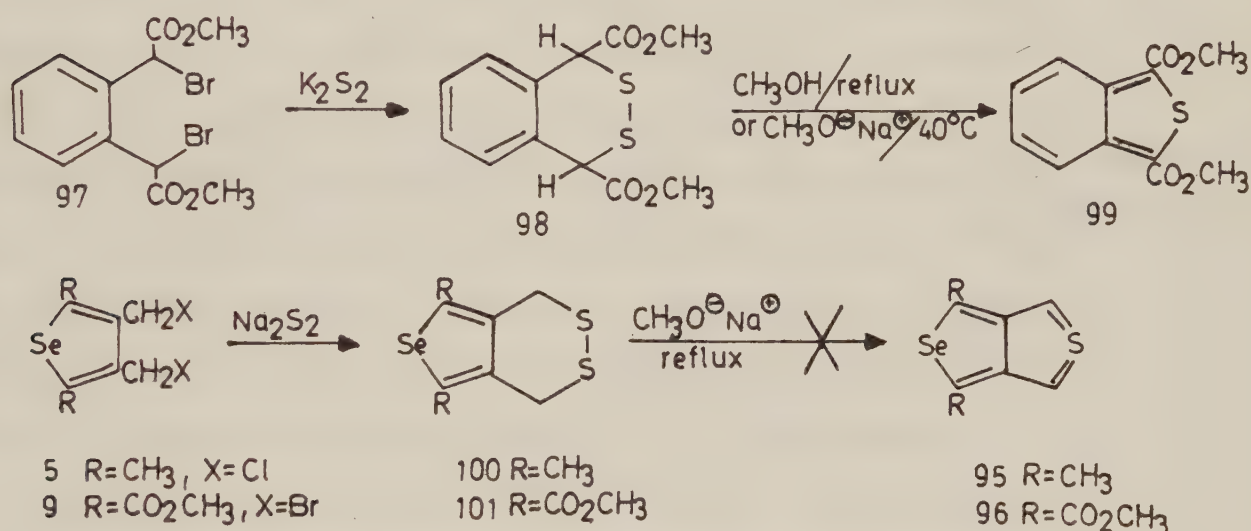
Saris and Cava³³ have also synthesized the dimethyl- and dicarbomethoxy-substituted selenium dibromides 81 and 82, respectively. Reductive debromination of 81 with 40 % sodium hydroxide solution resulted in the isolation of the ring-opened diselenide 88 and the selenide 71, 88 being isolated in the yield as high as 39 %. No formation of the nonclassical selenolothiophene 84 could be observed. In contrast, generation of the dicarbomethoxy derivative 85 from the dibromide 82, could be effected in CDCl_3 by the action of triethylamine. Our results indicate however, that reductive debromination of both the dimethyl- and dicarbomethoxy-substituted selenium dibromides 81 and 83 leads to the corresponding derivatives of the nonclassical selenolothiophene 84 and 86, respectively. Thus, addition of a few drops of NaOD solution in D_2O to a CDCl_3 solution of the dibromide 81, brought about generation of the selenolothiophene 84, as indicated by a singlet of the aromatic protons at δ 10.04 ppm. Simultaneously, the selenide 71 was also formed and after ca. 5 min the NMR spectrum indicated the presence of the nonclassical selenolothiophene 84, the starting dibromide 81 and the selenide 71 in a ratio of 1:3:5. After an additional hour, only the selenide 71 along with traces of the dibromide 81 and some unidentified decomposition products could be observed. A similar mixture

was also observed, when the debromination of the dicarbethoxy-substituted dibromide 83 was followed by NMR. The NMR spectra of both dibromides 81 and 83 in CDCl_3 showed the expected signals of the methylene protons at δ 4.95 and 5.35, respectively. If however, the spectra were recorded in DMSO-d_6 solution, decomposition of the dibromides into the selenides 71 and 75 started almost immediately. In both cases a rapidly down-field moving signal was also observed. Although it is reasonable to assume that this signal is due to the generation of hydrogen bromide and a shift change is caused by a variable concentration, no signals in the aromatic region, which could be attributed to the nonclassical selenolothiophenes 84 or 86, were observed.

As shown so far, the dienophile addition to the 1,3-disubstituted derivatives of the nonclassical selenolothiophene system takes place at the sites of highest electron density, independently of whether an adduct containing a sulfur or a selenium bridge is formed. Unfortunately, no adducts of the diphenyl-substituted compound 87 could, as yet, be obtained. It also seems, that the primary NPM-adducts containing a selenium bridge undergo a more facile aromatization to give a benzo[c]-thiophene derivative than the adducts with a sulfur bridge, which on aromatization would give a benzo[c]selenophene system. It was interesting to examine, if the above observations also apply to the 4,6-disubstituted derivatives of selenolo[3,4-c]thiophene, i.e. derivatives containing substituents in the selenophene part of the molecule. However, by far the most interesting question would be the behaviour of the unsubstituted and therefore unperturbed parent compound itself. 1H,3H-Thieno[3,4-c]-thiophene has been synthesized³² and shown to be a quite unstable compound.

We considered a similar synthesis of 4H,6H-selenolo[3,4-c]thiophene followed by oxidation and dehydratization to selenolo[3,4-c]thiophene to have limited chances of success, for which reason it was not yet undertaken. We have, however, synthesized the 4,6-dimethyl and 4,6-dicarbo-methoxy derivatives 89 and 91 by ring-closure of 3,4-bis(halomethyl)-selenophenes 5 and 9, respectively, with sodium sulfide in methanol. The synthetic path is shown in the lower part of Scheme 10 and will be extended to the 4,6-diphenyl derivative in the near future. Oxidation of the sulfides 89 and 91 gave the sulfoxides 93 and 94, dehydratization of which was hoped to bring about generation and possibly trapping of the 4,6-disubstituted selenolo[3,4-c]thiophenes 95 and 96. Indeed, heating of both sulfoxides to reflux in acetic anhydride gave rise to red coloration of the solution which remained unchanged during 2 hours in the case of 93 and 3 hours in the case of 94. These red colours, which we attribute to the nonclassical selenolothiophenes 95 and 96, respectively, vanished within a few minutes when a solution of N-phenylmaleimide in benzene was added. In both cases, the NPM-adducts were obtained in much better yields than for the 1,3-disubstituted derivatives. Their compositions were confirmed by the mass spectra but, unfortunately, no NMR spectra could be recorded owing to their low solubility in ordinary organic solvents. The NMR spectra obtained in warm DMSO- d_6 indicated only the presence of decomposition products. It is known, that thermal decomposition of the NPM-adducts of thieno[3,4-c]thiophene derivatives brings about a retro Diels-Alder reaction, but the NMR spectra obtained were not consistent with this concept. Further efforts to trap selenolothiophenes 95 and 96, as well as the diphenyl-substituted derivative, will be made.

We have also tried some other approaches to the nonclassical selenolothiophenes; one of them, which would lead to the above-mentioned derivatives 95 and 96, is shown in Scheme 11. Some years ago, Cignarella and Cordella^{34,35} have reported an alkali-induced decomposition of 1,4-dicarbomethoxy-2,3-benzodithiane (98) to give a benzo[c]thiophene derivative 99 in 90 % yield. This observation prompted us to examine if the selenolo-fused analogs of 99 would also decompose on treatment with sodium methoxide to give the nonclassical selenolothiophene derivatives.



Scheme 11

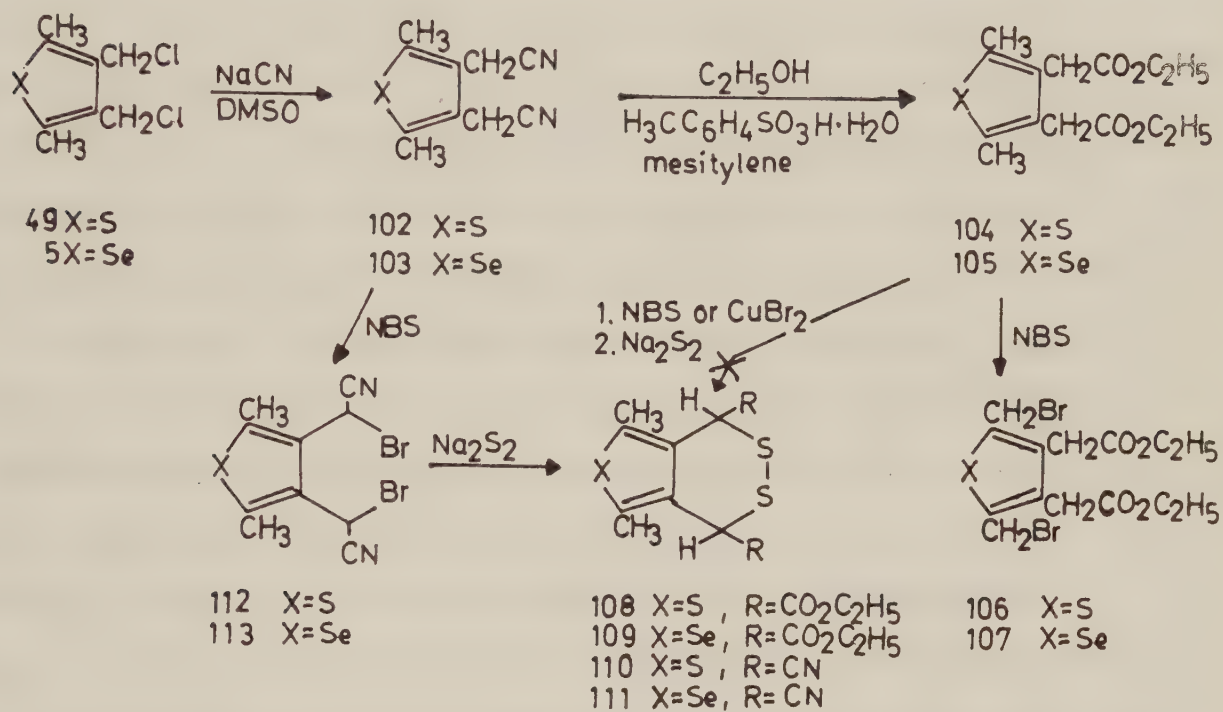
The benzodithiane 98 was synthesized by a ring-closure of the α,α' -dibromo diester 97 with methanolic potassium disulfide in 60 % yield.³⁴

Analogously, the ring-closure reaction of the 3,4-bis(halomethyl)selenophenes 5 and 9 afforded the required selenolo[3,4-d][1,2]dithianes 100 and 101 in 90 % and 71 % yields, respectively. Both compounds turned out to be very stable in refluxing methanol, under which conditions the benzodithiane 98 was converted into benzo c thiophene 99 within 1 hour in 91 % yield.³⁵

The conversion of 98 into 99 was also brought about by heating it to 40°C with an excess of 0.1 N methanolic CH₃ONa. Under these conditions and even when heated to reflux with sodium methoxide, the dimethyl-substituted selenolodithiane 100 was stable indefinitely, while compound 101 containing the carbomethoxy substituents decomposed within ca. 20 min of reflux into elemental selenium and some other unidentified products. However, no formation of the nonclassical selenolothiophene 96 could be observed and when the reaction was carried out in the presence of N-phenylmaleimide, no dienophile addition products were detected. We have also carried out similar experiments with the thieno analogs of the selenolodithianes 100 and 101, which would lead to the known derivatives of the nonclassical thieno[3,4-c]thiophene.² However, reflux with methanolic sodium methoxide for over 2 hours resulted in a quantitative recovery of the dimethyl-substituted thienodithiane, while the dicarbomethoxy derivative decomposed in a similar way as its selenolo analog 101.

Decomposition of 98 to a benzo[c]thiophene derivative 99 was shown to proceed via a thiolate anion.^{34,35} According to the authors, two driving forces appeared to be involved in this decomposition: (i) the inductive effect on the acidic carbon of the oxygenated substituents and (ii) the gain in energy on going from 98 to the fully aromatic structure 99. A possible explanation of the failure to generate the selenolothiophenes 95 and 96 by refluxing solutions of 100 and 101 in methanolic sodium methoxide, might thus be the lack of the electron-withdrawing carbomethoxy substituents in the dithiane compounds and/or an insufficient gain in energy due to the less aromatic character of the selenolothiophenes as compared to benzo[c]thiophene. Since we cannot influence the latter factor,

we have tried to introduce the carbomethoxy substituents into the 1,4-positions of the selenolodithiane structure along the route outlined in Scheme 12.



Scheme 12

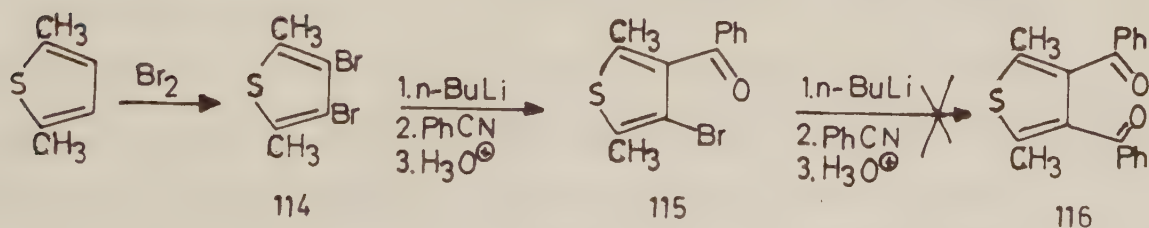
Reaction of the 3,4-bischloromethylthiophene 49 and -selenophene 5 with sodium cyanide in DMSO, according to the procedure of Friedman and Schechter,³⁶ afforded the known 3,4-biscyanomethylthiophene 102³⁷ and -selenophene 103 in 92 % (lit.³⁷: 49 %) and 90 % yields, respectively. Alcoholysis of the dinitrile 102 by an old Pinner method³⁸ has been reported to give the diester 104 in 45 % yield.³⁷ According to a newer procedure of James and Bryan,³⁹ the use of arenesulfonic acids as catalysts in the alcoholysis of nitriles, gives much better yields of esters. Indeed, when *p*-toluenesulfonic acid monohydrate was used, 104 and 105 could be obtained in 88 and 85 % yields, respectively. Unfortunately, subsequent NBS-bromination did not lead to the desired α -bromo esters, the ring-closure of which with sodium disulfide was hoped to give the 1,4-dicarbethoxy-substituted dithianes 108 and 109. The major products of the NBS-bromination were instead the 2,5-bisbromomethyl derivatives 106 and 107, along with lesser amounts of compounds brominated α to the ethereal oxygen. Neither did use of copper(II) bromide in chloroform - ethyl acetate, which was reported to selectively α -brominate ketones,⁴⁰ afford the required compounds.

Since ordinary esters usually do not brominate satisfactorily in the α -position, but rather react at the carbon α to the ethereal oxygen or at C-H bonds remote from the ester function, we have tried to brominate directly the nitriles 102 and 103. Subsequent ring-closure with sodium disulfide would then give 1,4-dicyano-substituted dithianes 110 and 111, in which the cyano groups could be expected to exert even stronger inductive effect than the ester groups. Unfortunately, the α -bromonitriles 112 and 113 turned out to be unstable and even when the NBS-bromination was immediately followed by addition of sodium disulfide, the desired dithianes 110 and 111

were not generated. A possible extension of this synthetic path could be hydrolysis of the esters groups of 104 and 105, followed by the Hell-Volhard-Zelinsky reaction of the diacids and alcoholic work-up to the α -bromo esters, but this route was not yet tested.

We have also tried some other approaches to the mixed sulfur-selenium systems, all of them with very limited success. In order to examine behaviour of the selenium analogs of compounds 100 and 101 on treatment with base, we have attempted the syntheses of both thieno- and selenolo-fused 1,2-diselenanes by ring-closure of 3,4-bishalomethylthiophenes or -selenophenes with sodium diselenide. However, in contrast to the very good yields obtained on ring-closure with sodium disulfide, the polymeric diselenides were obtained as major products in the reaction of 5, 9, 49 and 70 with sodium diselenide. Traces of the desired diselenanes were obtained when a high-dilution technique was applied.

In another approach, outlined in Scheme 13, 3-benzoyl-4-bromo-2,5-dimethylthiophene (115) was obtained from the thiophene 114 by treatment with *n*-butyllithium and benzonitrile followed by acidic work-up. However, the repeated treatment with *n*-butyllithium and benzonitrile did not afford the expected dibenzoyl compound 116, which was hoped to give the nonclassical thienothiophene 54 (cf. Scheme 7) on treatment with P_4S_{10}



Scheme 13

or 1,3-dimethyl-4,6-diphenylselenolo[3,4-c]thiophene on treatment with P_2Se_5 . When 115 was treated with *n*-butyllithium at $-70^\circ C$, the halogen-metal exchange was hindered, as indicated by the fact that only the starting material was recovered. When the lithiation was carried out at elevated temperatures, the ring-opening of the thiophene ring occurred. Similar attempts to prepare the 3,4-dibenzoyl-2,5-diphenylthiophene or -selenophene failed at even earlier stage, since the monobenzoyl-substituted compounds could not be obtained. Still another approach to the 3,4-dibenzoyl-substituted derivatives can be oxidation of the benzylic carbon atoms in 51, 52 or 53 (cf. Scheme 7), which however, was not yet tried.

CONCLUSIONS

Most of the projected synthetic routes to the nonclassical selenolo-selenophene and selenolothiophene systems tested in the present work have met with very limited or no success. Only the originally proposed acid-catalyzed dehydration of sulfoxides, used by Cava *et al.*² in their preparation of the thieno[3,4-c]thiophene derivatives, the similar dehydration of selenoxides, and the reductive, base-catalyzed debromination of selenium dibromides led to the generation of the above systems. Their transient existence is best demonstrated by trapping experiments with different 1,3-dipolarophiles, as well as by spectroscopic evidence. However, considerable difficulties have been encountered in isolation and consequently in characterization of the 1,3-adducts, in contrast to the behaviour of the sulfur analog - the thieno[3,4-c]thiophene system.² 1,3-Dipolar cycloaddition reaction of dimethyl acetylenedicarboxy-

late with derivatives of the selenolo[3,4-c]selenophene system led to the isolation of the double-sided addition and aromatization product 24 (cf. Scheme 4), which prevented the determination of the primary sites of addition. However, results obtained with the selenolothiophene system, both by Saris and Cava³³ and by the present authors, indicate that the dienophile addition takes place at the sites of highest electron density. It is reasonable to assume that the dienophile addition takes a similar course also with the selenolo[3,4-c]selenophene system. Further efforts to corroborate this assumption will be made.

EXPERIMENTAL

The NMR spectra were obtained with a Varian A-60 and on a JEOL MH 100 high resolution spectrometer. The IR spectra were recorded on a Perkin-Elmer model 257 instrument and the UV spectra on a Unicam SP 800 spectrophotometer. The gas chromatograph used was a Perkin-Elmer 900 instrument with flame ionization detector, connected to a Varian model 480 digital integrator. The integrator was not calibrated. Mass spectra were obtained with an LKB 9000 mass spectrometer and on a Finnigan model 4021 instrument.

Elementary analyses were carried out by Ilse Beetz, Mikroanalytisches Laboratorium, Kronach, Germany.

3,4-Bischloromethyl-2,5-dimethylselenophene (5). A fast stream of hydrogen chloride was led through a suspension of 120 g (4.00 mol) of paraformaldehyde in 500 ml of glacial acetic acid until a clear, colourless solution was obtained. 159 g (1.00 mol) of 2,5-dimethylselenophene⁹ was then added dropwise in 30 min into this solution under stirring and external cooling. After the addition was complete, the dark-green reaction mixture was stirred for 1.5 h, during which time the initially formed, light-green oil solidified. The solid was removed by filtration, washed with large amounts of water, and dried to give light-brown crystals, m.p. 65-68°C. Recrystallization from petroleum ether (b.p. 40-60°C) furnished 228 g (89 %) of golden-yellow needles, m.p. 71.5-73°C. NMR (CDCl₃): δ (ppm) 4.64 (s, 4H, CH₂), 2.50 (s, 6H, CH₃), $^3J_{-77\text{Se-CH}_3} = 11.0$ Hz.

Anal. Calcd. for C₈H₁₀Cl₂Se: C 37.53; H 3.94; Cl 27.69; Se 30.84.
Found: C 37.68; H 4.14; Cl 27.80; Se 30.55.

3,4-Bisiodomethyl-2,5-dimethylselenophene (6). To a solution of 6.4 g (0.025 mol) of 3,4-bischloromethyl-2,5-dimethylselenophene (5) in 50 ml of acetone, a solution of 8.1 g (0.055 mol) of sodium iodide in 100 ml of acetone was added with stirring at room temperature. After stirring for 3 hours, the precipitated sodium chloride was filtered off, the filtrate was concentrated in vacuo, and the half-crystalline residue obtained was recrystallized from petroleum ether (b.p. 40-60°C) to give 10.2 g (93 %) of the title compound, m.p. 97.5-98°C (decomp.). The bisiodomethylselenophene 6 is stable only for a few days at room temperature, but can be stored indefinitely in a refrigerator. NMR (CDCl₃): δ (ppm) 4.37 (s, 4H, CH₂), 2.35 (s, 6H, CH₃), $^3J_{-77\text{Se-CH}_3} = 10.5$ Hz.

Anal. Calcd. for C₈H₁₀I₂Se: C 21.89; H 2.30; Se 17.99.

Found: C 22.02; H 2.43; Se 17.87.

Dimethyl selenodiacetate (7). Aqueous sodium hydrogen selenide solution¹¹ prepared from 79 g (1.0 mol) of selenium and 80 g (2.1 mol) of sodium borohydride in 1 l of water under nitrogen was neutralized with 2 N hydrochloric acid to pH ~6 and 217 g (2.00 mol) of methyl chloroacetate was added dropwise with stirring at such a rate that the reaction mixture refluxed. After complete addition, the reaction mixture was stirred for 2 h at room temperature under nitrogen, and then extracted several times with ether. The combined ether extracts were washed with water, dried over magnesium sulfate and concentrated. The colourless residue was distilled under reduced pressure, giving 162 g (72 %) of the product, b.p. 144-145°C/15 mm Hg, as a colourless oil, which crystallized into large prisms, m.p. 24-25°C, upon standing in refrigerator. Lit.¹² b.p. 143°C/15 mm Hg.

2-Carboxy-5-carbomethoxy-3,4-dimethylselenophene (8). The title compound was prepared from 113 g (0.500 mol) of dimethyl selenodiacetate (7), 60.2 g (0.700 mol) of diacetyl, and 48 g (1.0 mol) of 50 % sodium hydride suspension, using the procedure described by Zwanenburg and Wynberg¹⁰ for the synthesis of the corresponding sulfur analog. Recrystallization of the crude reaction product from aqueous acetic acid (1:1) yielded 57.5 g (44 %) of the acid 8, m.p. 216-217°C. IR (KBr): 1720 and 1690 cm^{-1} (C=O). NMR (acetone- d_6): δ (ppm) 3.84 (s, 3H, CO_2CH_3), 2.44 (s, 6H, CH_3). Anal. Calcd. for $\text{C}_9\text{H}_{10}\text{O}_4\text{Se}$: C 41.40; H 3.86; Se 30.24. Found: C 41.55; H 3.92; Se 30.37.

2,5-Dicarbomethoxy-3,4-dimethylselenophene. To a solution of 52.2 g (0.200 mol) of the carboxylic acid 8 in 350 ml of HMPA, 12.0 g (0.300 mol) of sodium hydroxide in 36 ml of water was added and the solution was stirred at room temperature for one hour, whereupon 11.4 g (0.803 mol) of methyl iodide was added and the mixture was stirred over-night at room temperature. The solution was then poured into 1 l of 5 % hydrochloric acid and extracted several times with ether. The combined ether extracts were washed with sodium hydrogen carbonate and water, dried over magnesium sulfate and concentrated. Recrystallization of the residue from methanol gave 50.0 g (91 %) of the title compound, m.p. 161-162°C. IR (KBr): 1715 cm^{-1} (C=O). NMR (CDCl_3): δ (ppm) 3.85 (s, 6H, CO_2CH_3), 2.41 (s, 6H, CH_3). Anal. Calcd. for $\text{C}_{10}\text{H}_{12}\text{O}_4\text{Se}$: C 44.30; H 4.40; Se 29.82. Found: C 44.34; H 4.42; Se 29.69.

3,4-Bisbromomethyl-2,5-dicarbomethoxyselenophene (9). To a solution of 27.5 g (0.100 mol) of 2,5-dicarbomethoxy-3,4-dimethylselenophene in 350 ml of warm, dry carbon tetrachloride, 39.2 g (0.220 mol) of dry N-bromosuccinimide and ca. 100 mg of azobisisobutyronitrile were added

all at once and the reaction mixture was refluxed for 6 hours. The succinimide formed was removed by hot filtration, the filtrate was concentrated in vacuo and the half-crystalline residue obtained was recrystallized from ligroin to give 40.3 g (93 %) of the bis-bromomethylselenophene 9, m.p. 147-148°C. IR (KBr): 1715 cm^{-1} (C=O). NMR (CDCl_3): δ (ppm) 5.01 (s, 4H, CH_2), 3.90 (s, 6H, CO_2CH_3). Anal. Calcd. for $\text{C}_{10}\text{H}_{10}\text{Br}_2\text{O}_4\text{Se}$: C 27.74; H 2.33; Br 36.91; Se 18.27. Found: C 27.76; H 2.45; Br 36.80; Se 18.37.

4,6-Dimethyl-1H,3H-selenolo[3,4-c]selenophene (10). To a colourless solution of sodium hydrogen selenide,¹¹ prepared from 18.2 g (0.230 mol) of selenium and 9.6 g (0.25 mol) of sodium borohydride in 2 l of abs. ethanol, 51.2 g (0.200 mol) of solid 3,4-bischloromethyl-2,5-dimethylselenophene (5) was added in small portions over a period of 5 hours, with stirring at room temperature under nitrogen. After stirring over-night, the precipitated sodium chloride was filtered off and the filtrate was concentrated to ca. 250 ml and diluted with 0.5 l of water. The white suspension formed was extracted several times with chloroform, the combined chloroform extracts were washed with water and dried over magnesium sulfate. After evaporation of the solvent, the crystalline residue was subjected to steam-distillation, the distillate was extracted with chloroform, the organic phase extracts were washed with water, dried over magnesium sulfate and concentrated, yielding 23.7 g (45 %) of the title compound, m.p. 85-87°C. An analytical sample was obtained by recrystallization from methanol, m.p. 87-88°C. NMR (CDCl_3): δ (ppm) 3.68 (s, 4H, CH_2), 2.28 (s, 6H, CH_3), $^3J_{77}^{\text{Se-CH}_3} = 10.1 \text{ Hz}$, $^2J_{77}^{\text{Se-CH}_2} = 14.0 \text{ Hz}$.

In the mass spectrum, the peaks centred at m/e 266 (M^+ and base peak), showed the same pattern as a spectrum simulated for two selenium atoms. Anal. Calcd. for $C_8H_{10}Se_2$: C 36.38; H 3.82; Se 59.80. Found: C 36.34; H 3.84; Se 59.70.

The non-volatile residue after steam-distillation was dissolved in boiling chloroform, filtered and concentrated, giving 12.7 g (24 %) of 1,3,7,9-tetramethyl-4H,6H,10H,12H-diselenolo[3,4-c:3',4'-h]-[1,6]diselenecin (11), m.p. 192-194°C after recrystallization from large amounts of xylene. Owing to its low solubility in ordinary organic solvents, no NMR spectrum could be recorded. Both mass spectrum and the elementary analysis were in agreement with the dimeric structure of 11. In the mass spectrum, the peaks centred at m/e 532 (M^+) and at m/e 266 (base peak), showed the same pattern as a spectrum simulated for four and for two selenium atoms, respectively.

Anal. Calcd. for $C_{16}H_{20}Se_4$: C 36.38; H 3.82; Se 59.80. Found: C 36.55; H 3.96; Se 59.31.

4,6-Dicarbethoxy-1H,3H-selenolo[3,4-c]selenophene (12). To a colourless solution of sodium hydrogen selenide,¹¹ prepared from 7.1 g (0.090 mol) of selenium and 3.8 g (0.10 mol) of sodium borohydride in 1.5 l of abs. ethanol, 34.6 g (0.0803 mol) of solid 3,4-bisbromomethyl-2,5-dicarbomethoxyselenophene (9) was added in small portions over a period of 4 hours, with stirring at room temperature under nitrogen. After stirring over-night, the precipitated sodium bromide was filtered off and the filtrate was concentrated to ca. 200 ml and 400 ml of water was added. The yellow suspension formed was extracted several times with chloroform, the combined chloroform extracts were washed

with water and dried over magnesium sulfate. Evaporation of the solvent and recrystallization of the residue from large amounts of ligroin gave 26.7 g (88 %) of the title compound 12, m.p. 111-113°C. NMR (CDCl₃): δ (ppm) 4.30 (q, 4H, CH₂), 4.12 (s, 4H, CH₂), 1.35 (t, 6H, CH₃), $J_{\text{CH}_2\text{-CH}_3} = 7.05$ Hz.

In the mass spectrum, the peaks centred at m/e 382 (M^+), showed the same pattern as a spectrum simulated for two selenium atoms.

Anal. Calcd. for C₁₂H₁₄O₄Se₂: C 37.91; H 3.71; Se 41.54.

Found: C 37.97; H 3.88; Se 41.90.

From the non-soluble residue, 1.8 g (6 %) of 1,3,7,9-tetra-carbethoxy-4H,6H,10H,12H-diselenolo[3,4-c:3',4'-h][1,6 diselenecin](13) was obtained, m.p. 200-202°C after recrystallization from pyridine/water (10:1). Owing to its low solubility in ordinary organic solvents, no NMR spectrum could be recorded. Both mass spectrum and the elemental analysis were in agreement with the dimeric structure of 13. In the mass spectrum, the peaks centred at m/e 764 (M^+) and at m/e 382 (base peak), showed the same pattern as a spectrum simulated for four and two selenium atoms, respectively. Anal. Calcd. for C₂₄H₂₈O₈Se₄: C 37.91; H 3.71; Se 41.54. Found: C 38.12; H 3.85; Se 41.32.

4,6-Dimethyl-1H,3H-selenolo[3,4-c]selenophene-2-oxide (14). To a solution of 1.3 g (4.9 mmol) of the dihydroselenophene 10 in 25 ml of dry tetrahydrofuran cooled to -10°C in an ice-salt bath, a 3 % solution of hydrogen peroxide in dry THF was added dropwise with stirring under nitrogen. The reaction was monitored by TLC. After 10 min, a precipitate was formed and the supernatant became slightly pink. After 0.5 hour, the starting selenide was observed on TLC and additional hydrogen peroxide was added. After an additional hour of

stirring at -10°C , no selenide was detected by TLC and the reaction mixture was concentrated in vacuo and filtered to give 1.2 g (87 %) of the title compound, m.p. $97-99^{\circ}\text{C}$ (dec.), as a slightly pink powder. All attempts to purify the selenoxide by recrystallization resulted in decomposition accompanied by a development of an intense red-pink colour of the solution. In the mass spectrum, the molecular ion at m/e 282 was not observed, the highest observable peaks being centred at m/e 266 ($\text{M}^{+}-0$). These peaks showed the same pattern as a spectrum simulated for two selenium atoms, the whole spectrum being identical with that obtained for the selenide 10. IR spectrum and elementary analysis confirmed, however, the presence of the selenium-oxygen bonding in the molecule. IR (KBr): 800 cm^{-1} (Se-O). NMR (CDCl_3): δ (ppm) 3.87 (s, 4H, CH_2), 2.33 (s, 6H, CH_3). Anal. Calcd. for $\text{C}_8\text{H}_{10}\text{OSe}_2$: C 34.31; H 3.60; Se 56.38. Found: C 34.18; H 3.74; Se 56.20.

4,6-Dicarbethoxy-1H,3H-selenolo[3,4-c]selenophene-2-oxide (15).

A general procedure of Cinquini et al.¹³ for oxidation of selenides was used. A solution of 1.6 g (4.2 mmol) of the selenide 12 in a mixture of 170 ml of methanol, 50 ml of acetone and 20 ml of water was cooled to 0°C , while the selenide partially precipitated. To this cooled suspension, a 0.5 M solution of 1.0 g (4.7 mmol) of sodium metaperiodate in water was added dropwise with stirring under nitrogen. After stirring for one hour, the reaction mixture was diluted with water to dissolve the precipitated sodium iodate and the white suspension was extracted with chloroform. Addition of chloroform resulted in a development of the deep violet fluorescence of the organic phase, which remained unchanged during 5 hours under nitrogen. Upon attempted isolation of this violet product in the pure state, the selenide 12 along with some polymeric materials was obtained.

Oxidation of the selenide 12 with hydrogen peroxide in tetrahydrofuran at -10°C under nitrogen in the same manner as described above for the oxidation of 10, led directly to the development of the violet colour of the solution.

4,6-Dimethyl-1H,3H-selenolo[3,4-c]selenophene-2,2-dibromide (16).

To a cooled solution of 5.2 g (0.020 mol) of the dihydroselenophene 10 in 50 ml of dry carbon tetrachloride, a solution of 3.2 g (0.020 mol) of bromine in 30 ml of dry carbon tetrachloride was added dropwise with stirring over a period of 30 min, until the final drop of bromine left the reaction mixture slightly red. After complete addition, the reaction mixture was stirred for 15 min, the yellow precipitate formed was filtered off and dried giving 8.0 g (94 %) of the title compound, m.p. $118-120^{\circ}\text{C}$ (dec.). Attempts to recrystallize the dibromide resulted in decomposition. In the mass spectrum, the molecular ion at m/e 422, 426 was not observed, the highest observable peaks being centred at m/e 344 and 346 ($M^+-\text{Br}$). These peaks showed the same pattern as a spectrum simulated for two selenium and one bromine atom. Results of the elementary analysis confirmed, however, the presence of two bromine atoms in the molecule. NMR ($\text{DMSO}-d_6$): δ (ppm) 4.52 (s, 4H, CH_2), 2.48 (s, 6H, CH_3). Anal. Calcd. for $\text{C}_8\text{H}_{10}\text{Br}_2\text{Se}_2$: C 27.67; H 2.38; Br 37.70; Se 37.25. Found: C 22.77; H 2.48; Br 37.75; Se 37.19.

4,6-Dicarbethoxy-1H,3H-selenolo[3,4-c]selenophene-2,2-dibromide (17).

To a cooled solution of 3.0 g (7.9 mmol) of the selenide 12 in 40 ml of dry carbon tetrachloride, a solution of 1.3 g (8.1 mmol) of bromine in 20 ml of dry carbon tetrachloride was added dropwise with stirring over a period of 20 min, until the final drop of bromine left the solution slightly orange. On standing over-night, fine yellow crystals

of the title compound precipitated. The precipitate was filtered off and dried giving 3.9 g (92 %) of the dibromide, m.p. 149-151°C. In the mass spectrum, the molecular ion at m/e 538, 542 was not observed, the highest observable peaks being centred at m/e 460 and 462 (M^+-Br). These peaks showed the same pattern as a spectrum simulated for two selenium and one bromine atom. Results of the elemental analysis confirmed, however, the presence of two selenium atoms in the molecule. NMR (acetone- d_6): δ (ppm) 5.25 (s, 4H, CH_2), 4.40 (q, 4H, CH_2), 1.38 (t, 6H, CH_3), $J_{CH_2-CH_3} = 7.0$ Hz. Anal. Calcd. for $C_{12}H_{14}Br_2O_4Se_2$: C 26.69; H 2.61; Br 29.60; Se 29.25. Found: C 26.57; H 2.57; Br 31.40; Se 27.12.

1,3-Dimethylselenolo[3,4-c]selenophene (2). A solution of 1.1 g (3.9 mmol) of the selenoxide 14 in 40 ml of freshly distilled, degassed acetic anhydride was heated to reflux under nitrogen. After ca. 5 min of reflux, an intense red-violet colour of the solution developed and remained unchanged after an additional 3 hours of refluxing. Upon attempted isolation of this violet product in the pure state, the selenide 10 along with some polymeric materials was obtained. When a solution of 0.67 g (3.9 mmol) of N-phenylmaleimide in 15 ml of dry benzene was added to the acetic anhydride solution, the violet colour disappeared completely within 5 min and a few crystals of the NPM-adduct precipitated. The composition of the adduct was confirmed by its mass spectrum, which showed the major peaks at m/e 437 (M^+ , 6 %), 357 (M^+-Se , 5 %), 264 (M^+-NPM , 100 %), 184 ($M^+-NPM-Se$, 36 %), and 173 (NPM, 98 %). The peaks centred at m/e 437 and 264 showed the same pattern as a spectrum simulated for two selenium atoms and the peaks at m/e 357 and 184 - for one selenium atom.

1,3-Dicarbethoxyselenolo[3,4-c]selenophene (3). As described above, the selenoxide 15 could not be isolated in the pure state, both oxidation with sodium metaperiodate and hydrogen peroxide resulting in the development of the violet colour of the chloroform and tetrahydrofuran solutions, respectively (cf. above). When the extraction of the methanol-water suspension of the selenoxide 15 was carried out with benzene-d₆, the selenoloselenophene 3 was released into the upper benzene layer very rapidly, as shown by an immediate appearance of the violet colour. NMR spectrum of this C₆D₆ solution showed a single peak of the aromatic protons at δ 10.04 ppm, besides the quartet and the triplet of the carbethoxy groups at δ 4.35 and 1.36 ppm, respectively.

Extraction of the selenoxide suspension with *n*-hexane allowed us to record the UV spectrum, which showed $\lambda_{\text{max}} = 563 \text{ nm}$.

When a solution of N-phenylmaleimide in benzene was added to the violet benzene extracts of 3, the violet colour disappeared rapidly and a few crystals of the NPM-adduct precipitated. The composition of the adduct was confirmed by its mass spectrum, which showed the major peaks at m/e 533 (M^+ , 6 %), 473 ($M^+-\text{Se}$, 15 %), 380 ($M^+-\text{NPM}$, 80 %), 300 ($M^+-\text{NPM}-\text{Se}$, 100 %), and 173 (NPM, 62 %). The peaks centred at m/e 533 and 380 showed the same pattern as a spectrum simulated for two selenium atoms and the peaks at m/e 473 and 300 - for one selenium atom.

Reductive debromination of the selenium dibromides 16 and 17.

To 30 ml of 40 % sodium hydroxide solution cooled to 0°C, 1.4 g (3.3 mmol) of the selenium dibromide 16, or 1.8 g (3.3 mmol) of the selenium dibromide 17 was added with stirring under nitrogen. The initially yellow dibromides were decomposed within a few minutes forming white,

milky emulsions. When the resulting emulsions were stirred with *n*-hexane, selenoloselenophenes 2 and 3 respectively, were slowly released into the organic phase, which could be followed by the appearance of a deep violet colour remaining for over 2 hours in the case of 2 and for over 5 hours with 3. In both cases, the violet colour developed much faster when benzene was used as a solvent and vanished rapidly when a solution of *N*-phenylmaleimide in benzene was added. This yielded a few crystals of NPM-adducts with the mass spectra identical with those described above.

Adducts of 1,3-dimethylselenolo[3,4-*c*]selenophene (2) and 1,3-dimethylthieno[3,4-*c*]thiophene (21) with dimethyl acetylenedicarboxylate. A mixture of 560 mg (2.00 mmol) of the selenoxide 14 and 280 mg (1.97 mmol) of DMAD in 10 ml of acetic anhydride was refluxed under nitrogen for two hours. Evaporation of the solvent followed by crystallization from methanol/cyclohexane gave 176 mg (23 %) of 1,4-dimethyl-2,3,6,7-tetracarbomethoxynaphthalene (24), m.p. 241-243°C. Lit.¹⁴: m.p. 243-244°C.

The same tetracarbomethoxy naphthalene 24 was obtained in 34 % yield when a mixture of equimolar amounts of 4,6-dimethyl-1*H*,3*H*-thieno[3,4-*c*]thiophene-2-oxide² and DMAD in acetic anhydride was heated to reflux under nitrogen. NMR (CDCl₃): δ (ppm) 8.51 (s, 2H, H₅ and H₈), 3.98 (s, 6H, CO₂CH₃), 3.93 (s, 6H, CO₂CH₃), 2.75 (s, 6H, CH₃).

4,6-Dimethyl-1*H*,3*H*-selenolo[3,4-*c*]selenophene-2-dicyanomethylide (25). To a solution of 560 mg (2.00 mmol) of the selenoxide 14 in 40 ml of tetrahydrofuran, 258 mg (2.01 mmol) of tetracyanoethylene was added and the reaction mixture was refluxed for 2 hours under nitrogen. After cooling, the white precipitate was filtered off and dried giving

98 mg (15 %) of the title compound, m.p. 178-180°C. Concentration of the filtrate afforded 80 mg of the selenide 10 along with some polymeric materials showing no C≡N stretching vibrations. The selenonium dicyanomethylide structure of 25 was confirmed by its mass, IR and NMR spectra, as well as by elemental analysis. In the mass spectrum, the peaks centred at m/e 330 (M^+ , 15 %) and at m/e 266 ($M^+ - C(CN)_2$, 100 %), showed the same pattern as a spectrum simulated for two selenium atoms. IR (KBr): 2220 and 2260 cm^{-1} (C≡N). NMR (DMSO- d_6): δ (ppm) 4.38 (d, 2H, CH_2), 3.75 (d, 2H, CH_2), 2.23 (s, 6H, CH_3), $J_{\text{gem.}} = 16.2$ Hz. Anal. Calcd. for $\text{C}_{11}\text{H}_{10}\text{N}_2\text{Se}_2$: C 40.27; H 3.07; Se 48.13. Found: C 40.91; H 2.93; Se 47.84.

4,6-Dicarbethoxy-1H,3H-selenolo[3,4-c]selenophene-2-
-dicyanomethylide (26). To a solution of 380 mg (1.00 mmol) of the selenide 12 in 20 ml of dry tetrahydrofuran cooled to 5°C, 1.5 ml of a 3 % solution of hydrogen peroxide in dry tetrahydrofuran (30 % excess) was added dropwise with stirring under nitrogen. After stirring at 5°C for 5 min, a red-pink colour of the solution developed. After an additional period of 20 min, a solution of 128 mg (1.00 mmol) of tetracyanoethylene in 5 ml of dry tetrahydrofuran was added, whereupon the colour changed to yellow and white precipitate formed. The precipitate was filtered off and dried giving 63 mg (14 %) of the title compound, m.p. 191-193°C. Concentration of the filtrate afforded 85 mg of the selenide 12 along with some polymeric materials exhibiting no C≡N stretching vibrations. The selenonium dicyanomethylide structure of 26 was confirmed by its mass, IR and NMR spectra, as well as by elemental analysis. In the mass spectrum the peaks centred at m/e 446 (M^+ , 13 %) and at m/e 382 ($M^+ - C(CN)_2$, 100 %), showed the same pattern as a

spectrum simulated for two selenium atoms. IR (KBr): 2210 and 2255 cm^{-1} ($\text{C}\equiv\text{N}$). NMR ($\text{DMSO}-d_6$): δ (ppm) 4.83 (d, 2H, CH_2), 4.33 (q, 4H, CH_2), 4.09 (d, 2H, CH_2), 1.37 (t, 6H, CH_3), $J_{\text{CH}_2-\text{CH}_3} = 7.2$ Hz, $J_{\text{gem.}} = 16.5$ Hz. Anal. Calcd. for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_4\text{Se}_2$: C 40.56; H 3.18; Se 35.55. Found: C 40.61; H 3.11; Se 35.44.

3,4-Dimethyl-2,5-diphenylselenophene (34). A mixture of 7.0 g (0.030 mol) of 2,3-dimethyl-1,4-diphenyl-1,3-butadiene (32)⁴¹ and 4.0 g (0.051 mol) of selenium in 30 ml of xylene was heated at 300°C in a sealed, heavy-walled glass ampoule placed in a closed metal cylinder for 16 hours. The ampoule was then broken, the excess of selenium was filtered and washed with warm chloroform and the combined organic phases were concentrated in vacuo. The light-brown, oily residue obtained solidified upon standing over-night. Recrystallization from ligroin afforded 4.9 g (52 %) of the title compound, m.p. 157.5-158°C, with all spectroscopic data in accordance with those obtained for 34 prepared by ring-closure of 2,3-dimethyl-1,4-diphenyl-1,4-butanedione (31) with phosphorus pentaselenide.⁹

A similar reaction of the butadiene 32 with sulfur afforded 3,4-dimethyl-2,5-diphenylthiophene (33) in 48 % yield, m.p. 157-159°C (ligroin). Lit.²³: 160°C (benzene).

3,4-Bisbromomethyl-2,5-diphenylselenophene (36). To a solution of 3.11 g (10.0 mmol) of 3,4-dimethyl-2,5-diphenylselenophene (34) in 80 ml of dry carbon tetrachloride, 3.92 g (22.0 mmol) of dry N-bromosuccinimide was added and the reaction mixture was irradiated with an OSRAM Ultra-Vitalux 300 W lamp for two hours until nearly all NBS was converted into succinimide. The succinimide was then filtered off and the red filtrate concentrated in vacuo to give a light-brown, oily residue, which solidified on standing. Recrystallization from ligroin gave 4.52 g

(96 %) of the title compound, m.p. 116-118⁰C. NMR (CDCl₃): δ (ppm) 7.67-7.35 (m, 10H, C₆H₅), 4.64 (s, 4H, CH₂). Anal. Calcd. for C₁₈H₁₄Br₂Se: C 46.09; H 3.01; Se 16.83. Found: C 46.55; H 3.21; Se 16.25.

A similar NBS bromination of the thiophene 33 gave 3,4-bisbromo-methyl-2,5-diphenylthiophene (35) in 93 % yield, m.p. 111-113⁰C (from ligroin). Lit.²³: 112⁰C (acetone).

4,6-Diphenyl-1H,3H-selenolo[3,4-c]selenophene (37). To a colourless solution of sodium hydrogen selenide,¹¹ prepared from 0.87 g (0.011 mol) of selenium and 0.46 g (0.012 mol) of sodium borohydride in 250 ml of abs. ethanol, 4.69 g (0.010 mol) of solid 3,4-bisbromomethyl-2,5-diphenylselenophene (36) was added in small portions during 3 hours with stirring under nitrogen. After complete addition, the reaction mixture was refluxed for 20 min and stirred over-night at room temperature. The precipitated sodium bromide was filtered off and washed thoroughly with warm ethanol. The combined ethanol phases were concentrated and the resulting, half-crystalline, yellow residue was recrystallized from ethanol giving 1.87 (48 %) of the title compound, m.p. 127-129⁰C. NMR (DMSO-d₆): δ (ppm) 7.63-7.16 (m, 10H, C₆H₅), 4.02 (s, 4H, CH₂).

In the mass spectrum, the peaks centred at m/e 390 (M⁺), showed the same pattern as a spectrum simulated for two selenium atoms.

From the non-soluble residue, 0.54 (14 %) of 1,3,7,9-tetraphenyl-4H,6H,10H,12H-diselenolo[3,4-c:3',4'-h] [1,6]diselenecin (38) was obtained, m.p. >340⁰C after recrystallization from xylene. Owing to its low solubility in ordinary organic solvents, no NMR spectrum could be recorded. In the mass spectrum, the peaks centred at m/e 780 (M⁺) and at m/e 390 (base peak), showed the same pattern as a spectrum simulated for four and for two selenium atoms, respectively.

4,6-Diphenyl-1H,3H-selenolo[3,4-c]selenophene-2-oxide (39).

To a solution of 0.97 g (2.5 mmol) of the dihydroselenophene 37 in 50 ml of dry tetrahydrofuran cooled to 5°C, a 5 % solution of hydrogen peroxide in dry THF was added dropwise with stirring under nitrogen. The reaction was monitored by TLC and the addition of hydrogen peroxide was continued until no more starting selenide was detected. After standing over-night at 4°C, the white precipitate formed was filtered off and dried to give 0.81 g (80 %) of the title compound, m.p. 120-124°C (dec.). All attempts to recrystallize the selenoxide resulted in decomposition. In the mass spectrum, the molecular ion at m/e 406 was not observed, the highest observable peaks being centred at m/e 390 (M^+-O). These peaks showed the same pattern as a spectrum simulated for two selenium atoms, the whole spectrum being identical with that obtained for the selenide 37. NMR (DMSO- d_6): δ (ppm) 7.68-7.34 (m, 10H, C_6H_5), 4.12 (s, 4H, CH_2). In the IR spectrum, the Se-O stretching vibrations were observed as a strong band at 815 cm^{-1} . No satisfactory elementary analysis could be obtained.

4,6-Diphenyl-1H,3H-selenolo[3,4-c]selenophene-2,2-dibromide (40).

To a solution of 0.97 g (2.5 mmol) of the selenide 37 in 40 ml of methylene chloride, a solution of 0.40 g (2.5 mmol) of bromine in 15 ml of methylene chloride was added dropwise with stirring at room temperature, until the final drop of bromine solution left the reaction mixture slightly red. After stirring for 3 hours, the yellow precipitate formed was filtered off and dried giving 1.22 g (89 %) of the title compound, m.p. 187-191°C (dec.). Attempts to purify the dibromide by recrystallization resulted in decomposition. In the mass spectrum, the molecular ion at m/e 546, 550 was not observed, the highest observable peaks being

centred at m/e 468 and 470 (M^+-Br). These peaks showed the same pattern as a spectrum simulated for two selenium and one bromine atom. NMR ($DMSO-d_6$): δ (ppm) 7.76-7.38 (m, 10H, C_6H_5), 4.87 (s, 4H, CH_2). No satisfactory elementary analysis could be obtained.

1,3-Diphenyl-4H,6H-selenolo[3,4-c]thiophene (43). To a colourless solution of sodium hydrogen selenide,¹¹ prepared from 0.87 g (0.011 mol) of selenium and 0.46 g (0.012 mol) of sodium borohydride in 250 ml of abs. ethanol, 4.22 (0.010 mol) of solid 3,4-bisbromomethyl-2,5-diphenylthiophene (35) was added in small portions during 2 hours with stirring under nitrogen. After complete addition, the reaction mixture was heated to reflux for 0.5 hour and stirred over-night at room temperature. The precipitated sodium bromide was filtered off and washed thoroughly with warm ethanol. The combined ethanol phases were concentrated to about 50 ml and poured into 0.5 l of water. The resulting white suspension was extracted with chloroform, the combined extracts were dried over magnesium sulfate and concentrated, affording 2.22 g (65 %) of a yellow, crystalline residue, the mass spectrum of which indicated the presence of the dimeric diselenecin along with the desired 43. Fractional crystallization from ethanol gave 1.31 g (38 %) of the title compound, m.p. 125-127°C. NMR ($CDCl_3$): δ (ppm) 7.56-7.21 (m, 10H, C_6H_5), 4.08 (s, 4H, CH_2), $^3J_{77Se-CH_2} = 14.4$ Hz. In the mass spectrum, the peaks centred at m/e 342 (M^+), showed the same pattern as a spectrum simulated for one sulfur and one selenium atom.

Anal. Calcd. for $C_{18}H_{19}SSe$: C 63.34; H 4.13; Se 23.13.
Found: C 62.81; H 4.08; Se 24.01.

From the non-soluble residue, 0.62 g (18 %) of 1,3,7,9-tetra-phenyl-4H,6H,10H,12H-dithieno[3,4-c:3',4'-h][1,6]diselenecin (77) was obtained, m.p. $>330^{\circ}\text{C}$ after recrystallization from xylene. Owing to its low solubility in ordinary organic solvents, no NMR spectrum could be recorded. In the mass spectrum, the peaks centred at m/e 684 (M^{+}) and at m/e 342 (base peak), showed the same pattern as a spectrum simulated for two sulfur and two selenium atoms and for one sulfur and one selenium atom, respectively.

1,3-Diphenyl-4H,6H-selenolo[3,4-c]thiophene-5-oxide (44). To a solution of 1.71 g (5.00 mmol) of the dihydroselenolothiophene 43 in 50 ml of dry tetrahydrofuran cooled to 5°C , a 5 % solution of hydrogen peroxide in dry THF was added dropwise with stirring under nitrogen. The reaction was monitored by TLC and the addition was continued until no more starting selenide was detected. After standing over-night at 4°C , the white precipitate formed was filtered off and dried to give 1.52 g (85 %) of the title compound, m.p. $118-121^{\circ}\text{C}$. All attempts at purification resulted in decomposition of the selenoxide. In the mass spectrum, the molecular ion at m/e 358 was not observed, the highest observable peaks being centred at m/e 342 ($M^{+}-0$). These peaks showed the same pattern as a spectrum simulated for one selenium and one sulfur atom, the whole spectrum being identical with that obtained for the selenide 43. NMR ($\text{DMSO}-d_6$): δ (ppm) 7.72-7.23 (m, 10H, C_6H_5), 4.16 (s, 4H, CH_2). IR (KBr): 820 cm^{-1} (Se-O). No satisfactory elementary analysis could be obtained.

1,3-Diphenyl-4H,6H-selenolo[3,4-c]thiophene-5,5-dibromide (45).

To a solution of 1.71 g (5.00 mmol) of the dihydroselenolothiophene 43 in 40 ml of methylene chloride, a solution of 0.83 g (5.2 mmol) of bromine in 15 ml of methylene chloride was added dropwise with stirring at room temperature, until the final drop of bromine solution left the reaction mixture slightly red. On standing over-night, the orange precipitate formed was filtered off and dried to give 2.2 g (88 %) of the title compound, m.p. 174-178°C (dec.). All attempts at purification resulted in decomposition of the dibromide. In the mass spectrum, the molecular ion at m/e 498, 502 was not observed, the highest observable peaks being centred at m/e 420 and 422 (M^+-Br). These peaks showed the same pattern as a spectrum simulated for two selenium and one bromine atom. NMR (DMSO- d_6): δ (ppm) 7.88-7.32 (m, 10H, C_6H_5), 4.94 (s, 4H, CH_2). No satisfactory elementary analysis could be obtained.

1,3-Diphenylselenolo[3,4-c]selenophene (4). A solution of 404 mg (1.00 mmol) of the selenoxide 39 in 3 ml of freshly distilled, degassed acetic anhydride was heated to reflux under nitrogen. After ca. 10 min of heating, an intense red-pink colour of the solution developed. Upon attempted isolation in the pure state, the selenide 37 along with some polymeric materials were obtained. When a solution of 173 mg (1.00 mmol) of N-phenylmaleimide in 4 ml of acetic anhydride was added, the red colour disappeared rapidly and a few crystals of the NPM-adduct precipitated on cooling. The composition of the adduct was confirmed by its mass spectrum, which showed the major peaks at m/e 561 (M^+ , 4 %), 481 (M^+-Se , 5 %), 388 (M^+-NPM , 100 %), 308 ($M^+-NPM-Se$, 42 %) and 173 (NPM, 84 %). The peaks centred at m/e 561 and 388 showed the same pattern as a spectrum simulated for two selenium atoms and the peaks at m/e 481 and 308 - for one selenium atom.

3,4-Dibenzyl-2,5-diphenylthiophene (52). To a solution of 1.27 g (3.01 mmol) of 3,4-bisbromomethyl-2,5-diphenylthiophene (35)²³ in 15 ml of dry benzene, 0.40 g (3.00 mmol) of anhydrous aluminium chloride was added in small portions with stirring and external cooling in an ice-water bath. The originally light-yellow reaction mixture became brown and an additional 10 ml of benzene was added. After complete addition, stirring was continued for 20 min and the reaction mixture was left over-night. 80 ml of 2 N hydrochloric acid was added, the benzene layer was separated and the water phase was extracted with benzene. The combined organic phases were washed with sodium hydrogen carbonate and water and dried over magnesium sulfate. Evaporation of the solvent and recrystallization from cyclohexane gave 0.76 g (61 %) of the title compound, m.p. 147-150°C. Lit.²⁵: 151°C (ethanol). NMR (CDCl₃): δ (ppm) 7.56-7.12 (m, 20, C₆H₅), 3.84 (s, 4H, CH₂).

3,4-Dibenzyl-2,5-diphenylselenophene (53). To a stirred, ice-cooled solution of 1.41 g (3.00 mmol) of 3,4-bisbromomethyl-2,5-diphenylselenophene (36) in 25 ml of dry benzene, 0.40 g (3.00 mmol) of anhydrous aluminium chloride was added in small portions during 1.5 hours. The originally yellow reaction mixture became dark brown and was diluted with an additional 10 ml of benzene. After standing over-night, the mixture was decomposed with 80 ml of ice-cold 2 N hydrochloric acid whereupon a red colour of solution developed. After stirring for 30 min, the benzene layer was separated, the water phase was extracted with benzene and the combined organic phases were washed with sodium hydrogen carbonate and water and dried over magnesium sulfate. Evaporation of the solvent and recrystallization from cyclo-

hexane afforded 0.65 g (47 %) of the title compound, m.p. 149-151°C. Lit.²⁵: 148°C (acetic acid). NMR (CDCl₃): δ (ppm) 7.50-6.74 (m, 20H, C₆H₅), 3.91 (s, 4H, CH₂).

NBS bromination of 3,4-dibenzyl-2,5-dimethylthiophene (51). To a solution of 585 mg (2.00 mmol) of the dibenzylthiophene 51²⁶ in 10 ml of dry carbon tetrachloride, 712 mg (4.00 mmol) of N-bromosuccinimide and ca. 50 mg of azobisisobutyronitrile were added all at once and the reaction mixture was refluxed for 1 hour. The succinimide formed was removed by hot filtration, the yellow filtrate was concentrated in vacuo and the residue obtained was recrystallized from petroleum ether (b.p. 60-85°C) to give 624 mg (69 %) of light yellow crystals, m.p. 57-60°C, the NMR spectrum of which was consistent with a compound brominated in the two methyl groups and not in the benzylic positions. NMR (CDCl₃): δ (ppm) 7.32-6.89 (m, 10H, C₆H₅), 4.56 (s, 4H, CH₂), 3.78 (s, 4H, CH₂).

Similar brominations of the dibenzyl thiophene 52 and selenophene 53 gave the mixtures of starting materials (ca. 70 % recovery) and some not identified, bromine-containing products.

Reactions of 51, 52 and 53 with sulfur at 300°C according to Ref. 25, led to destruction of the starting materials, although in the case of 52, traces of the carbocyclization product, 10,11-diphenyl-diindeno-[1,2-b:2',1'-d]thiophene, m/e 412 (M⁺, C₃₀H₂₀S), were obtained by chromatography of the product mixture on neutral alumina. In the reaction of 53 with sulfur, the corresponding diindeno-selenophene was not detected.

6-Bromo-5,7-dioxo-6,7-dihydro-5H-dibenzo[a,c]cycloheptene (68).

To a suspension of 2.23 g (10.0 mmol) of 5,7-dioxo-6,7-dihydro-5H-dibenzo[a,c]cycloheptene (67)²⁹ in 60 ml of acetic acid cooled to 12°C, a solution of 1.58 g (9.88 mmol) of bromine in 30 ml of acetic acid was added dropwise with efficient stirring to prevent freezing of the solvent. After an additional hour of stirring, the reaction mixture was poured into 1 l of water and the yellow precipitate formed was filtered off and dried to give 2.8 g (93 %) of the title compound, m.p. 160-164°C. An analytically pure sample, m.p. 164-166°C, was obtained by recrystallization from toluene. IR (KBr): 1685 cm⁻¹ (C=O). NMR (DMSO-d₆): δ (ppm) 8.12-7.97 (m, 2H, H₄ and H₈), 7.88-7.75 (m, 2H, H₃ and H₉), 7.62-7.47 (m, 4H, H₁, H₂, H₁₀ and H₁₁), 6.23 (s, 1H, H₆). Anal. Calcd. for C₁₅H₉BrO₂: C 59.83; H 3.01; Br 26.53. Found: C 59.90; H 3.11; Br 26.35.

Thallium(I) salt of 5,7-dioxo-6,7-dihydro-5H-dibenzo[a,c]cycloheptene (69). To a stirred solution of 2.23 g (10.0 mmol) of the dione 67 in 80 ml of ethanol, 2.50 g (10.0 mmol) of thallium(I) ethoxide was added all at once, the reaction mixture was stirred for 5 min and left in a refrigerator over-night. The yellow precipitate formed was filtered off and dried to give 3.8 g (89 %) of the title compound, decomposing without melting over 145°C.

6,6'-Bis-(5,7-dioxo-6,7-dihydro-5H-dibenzo[a,c]cycloheptene) (62).

A suspension of 2.13 g (5.00 mmol) of the thallium salt 69 and 1.51 g (5.01 mmol) of the monobromo cycloheptenedione 68 in 200 ml of ligroin was heated under reflux with stirring for 4 hours. Hot filtration and cooling of the light-yellow ligroin filtrate afforded 1.15 g of the title compound as yellow prisms, m.p. 85-88°C. Extraction of the red-brown

residue after filtration with boiling chloroform, evaporation of the solvent and recrystallization from ligroin gave an additional 2.12 g (74 %) of the compound. In the mass spectrum, the molecular ion at m/e 442 was not observed, the highest peak being at m/e 440 ($M^+ - 2H$). NMR ($CDCl_3$): δ (ppm) 7.55-7.32 (m, 16H, C_6H_5), 4.03 (s, 2H, CH).

Anal. Calcd. for $C_{30}H_{18}O_4$: C 81.44; H 4.10. Found: C 80.80; H 3.98.

1,3-Dimethyl-4H,6H-selenolo[3,4-c]thiophene (71). To a colourless solution of sodium hydrogen selenide,¹¹ prepared from 4.58 g (0.0580 mol) of selenium and 2.39 g (0.0631 mol) of sodium borohydride in 750 ml of abs. ethanol, 10.5 g (0.0502 mol) of solid 3,4-bischloromethyl-2,5-dimethylthiophene (49)³¹ was added in small portions during 4 hours, with stirring at room temperature under nitrogen. After stirring overnight, the precipitated sodium chloride was filtered off and the filtrate was concentrated in vacuo. The half-crystalline residue obtained was subjected to steam distillation. The distillate was extracted with chloroform, the chloroform extracts were dried over magnesium sulfate and concentrated yielding 5.4 g (50 %) of the title compound, m.p. 70-71.5°C, after recrystallization from methanol.

Lit.³³ m.p. 66-67°C after sublimation, 60 %. NMR ($CDCl_3$): δ (ppm) 3.78 (s, 4H, CH_2), 2.21 (s, 3H, CH_3), $^2J_{77}^{Se-CH_2} = 14.2$ Hz.

Anal. Calcd. for $C_8H_{10}SSe$: C 44.24; H 4.64; Se 36.35. Found: C 44.24; H 4.87; Se 36.25.

The non-volatile residue after steam distillation was dissolved in boiling chloroform, filtered and concentrated, giving 1.7 g (16 %) of 1,3,7,9-tetramethyl-4H,6H,10H,12H-dithieno[3,4-c:3',4'-h][1,6]-diselenecin (72), m.p. 195-197°C, after recrystallization from toluene. Lit.³³ m.p. 165-166°C. Owing to its low solubility in ordinary organic

solvents, no NMR spectrum could be recorded. Anal. Calcd. for $C_{16}H_{20}S_2Se_2$: C 44.24; H 4.64; Se 36.35. Found: C 43.43; H 4.48; Se 37.10.

1,3-Dicarbethoxy-4H,6H-selenolo[3,4-c]thiophene (75). To a colourless solution of sodium hydrogen selenide,¹¹ prepared from 1.74 g (0.0220 mol) of selenium and 0.95 g (0.0251 mol) of sodium borohydride in 350 ml of ethanol, 7.72 g (0.0200 mol) of solid 3,4-bisbromomethyl-2,5-dicarbomethoxythiophene (70)³² was added in small portions during 4 hours, with stirring at room temperature under nitrogen. After stirring over-night, the precipitated sodium bromide was filtered off and the filtrate was concentrated to ca. 100 ml and diluted with 300 ml of water. The yellow suspension formed was extracted several times with chloroform, the combined chloroform extracts were washed with water, dried over magnesium sulfate and concentrated. Recrystallization from ethanol afforded 4.5 g (68 %) of the title compound, m.p. 110-112°C. The corresponding dimethyl ester 73 was obtained by Saris and Cava³³ in 88 % yield, m.p. 165-166°C after sublimation. NMR ($CDCl_3$): δ (ppm) 4.35 (q, 4H, CH_2), 4.19 (s, 4H, CH_2), 1.37 (t, 6H, CH_3), $J_{CH_2-CH_3} = 7.0$ Hz. Anal. Calcd. for $C_{12}H_{14}O_4SSe$: C 43.25; H 4.23; Se 23.69. Found: C 43.43; H 4.04; Se 23.84.

From the non-soluble residue, 0.8 g (12 %) of 1,3,7,9-tetracarb-ethoxy-4H,6H,10H,12H-dithieno[3,4-c:3',4'-h][1,6]diselenecin (76) was obtained, m.p. 198-201°C, after recrystallization from acetone. Owing to its low solubility in ordinary organic solvents, no NMR spectrum could be recorded. The corresponding tetracarbomethoxydiselenecin 74³³ melted at 216-220°C. Anal. Calcd. for $C_{24}H_{28}O_8S_2Se_2$: C 43.25; H 4.23; Se 23.69. Found: C 42.34; H 4.18; Se 24.79.

1,3-Dimethyl-4H,6H-selenolo[3,4-c]thiophene-5-oxide (78). To a solution of 2.17 g (0.0100 mol) of the selenide 71 in 10 ml of dry tetrahydrofuran cooled to -10°C , a 20 % excess of a 5 % solution of hydrogen peroxide in dry THF was added dropwise with stirring under nitrogen. After 1.5 hours of stirring at 0°C , the reaction mixture was concentrated in vacuo and filtered to give 2.15 g (92 %) of the title compound, m.p. $109-110^{\circ}\text{C}$. Lit.³³ m.p. $108-110^{\circ}\text{C}$, 99 %. All attempts at purification resulted in decomposition accompanied by a development of a red-pink colour of the solution. NMR (CDCl_3): δ (ppm) 3.94 (s, 4H, CH_2), 2.27 (s, 6H, CH_3), $^2J_{-77\text{Se}-\text{CH}_2} = 14.0$ Hz. If the NMR spectrum was recorded in DMSO-d_6 immediately after dissolving the compound, the expected signal of the methylene and methyl protons appeared as two singlets at δ 4.27 and 2.34, respectively. If, however, the spectrum was recorded after a short period of time or after slight warming of the DMSO solution, the intensity of both signals diminished, two new signals at δ 10.04 and 2.68 arising. These signals, which we attribute to the nonclassical selenolothiophene 84, increased to about the same intensity as those for the selenoxide, and remained unchanged for over 5 hours. More than 50 % conversion was, however, not observed. No satisfactory elemental analysis could be obtained.

1,3-Dicarbethoxy-4H,6H-selenolo[3,4-c]thiophene-5-oxide (80). To a solution of 333 mg (1.00 mmol) of the selenide 75 in 10 ml of dry tetrahydrofuran cooled to -10°C , a 25 % excess of a 5 % solution of hydrogen peroxide in dry THF was added dropwise with stirring under nitrogen. An initially formed, white precipitate redissolved after ca. 15 min of stirring and a red-pink colour of the solution developed. This colour remained unchanged for an additional hour of stirring at -10°C ,

after which time a solution of 128 mg (1.00 mmol) of tetracyanoethylene in 5 ml of THF was added dropwise. The colour changed to yellow within 30 seconds and a white precipitate formed. The precipitate was filtered off and dried giving 75 mg (19 %) of the compound, m.p. 161-164°C, for which all spectroscopic data and the results of the elemental analysis, indicated a structure of 1,3-dicarbethoxy-4H,6H-selenolo[3,4-c]thiophene-5,5-dicyanomethylide. IR (KBr): 2210 and 2255 cm^{-1} ($\text{C}\equiv\text{N}$). NMR (DMSO-d_6): δ (ppm) 4.91 (d, 2H, CH_2), 4.38 (q, 4H, CH_2), 4.16 (d, 2H, CH_2), 1.39 (q, 6H, CH_3), $J_{\text{CH}_2-\text{CH}_3} = 7.2$ Hz, $J_{\text{gem.}} = 16.5$ Hz. Anal. Calcd. for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_4\text{SSe}$: C 45.35; H 3.55; Se 19.87. Found: C 46.41; H 3.47; Se 20.21.

1,3-Dimethyl-4H,6H-selenolo[3,4-c]thiophene-5,5-dibromide (81).

To a cooled solution of 652 mg (3.00 mmol) of the selenide 71 in 5 ml of dry carbon tetrachloride, a solution of 485 mg (3.03 mmol) of bromine in 5 ml of dry carbon tetrachloride was added dropwise with stirring, until the final drop of bromine left the solution slightly orange. After an additional 0.5 hour of stirring, the bright-yellow precipitate was filtered off and dried to give 1.10 g (97 %) of the title compound, m.p. 128-131°C. Lit.³³ m.p. 132-135°C, 92 %. NMR (CDCl_3): δ (ppm) 4.95 (s, 4H, CH_2), 2.28 (s, 6H, CH_3). If the spectrum was recorded in DMSO-d_6 solution, decomposition of the dibromide into the starting selenide 71 and some other decomposition products was observed. Anal. Calcd. for $\text{C}_8\text{H}_{10}\text{Br}_2\text{SSe}$: C 25.49; H 2.67; Se 20.94; Br 42.39. Found: C 25.50; H 2.59; Se 21.21; Br 43.83.

1,3-Dicarbethoxy-4H,6H-selenolo[3,4-c]thiophene-5,5-dibromide (83).

To a cooled solution of 333 mg (1.00 mmol) of the selenide 75 in 5 ml of dry carbon tetrachloride, a solution of 165 mg (1.03 mmol) of bromine in 5 ml of dry carbon tetrachloride was added dropwise with stirring, until

the final drop left the solution slightly orange. After an additional 0.5 hour of stirring, the yellow precipitate was filtered off and dried, giving 390 mg (79 %) of the title compound, m.p. 143-145°C. The corresponding selenium dibromide 82 bearing carbomethoxy groups was obtained by Saris and Cava³³ in 43 % yield, m.p. 180°C. NMR (CDCl₃): δ (ppm) 5.35 (s, 4H, CH₂), 4.39 (q, 4H, CH₂), 1.39 (t, 6H, CH₃), $J_{\text{CH}_2-\text{CH}_3} = 7.0$ Hz. Anal. Calcd. for C₁₂H₁₄Br₂O₄SSe: C 29.23; H 2.86; Br 32.41; Se 16.01. Found: C 29.07; H 2.89; Br 31.78; Se 16.41.

1,3-Dimethylselenolo[3,4-c]selenophene (84). A solution of 233 mg (1.00 mmol) of the selenoxide 78 in 7 ml of freshly distilled, degassed acetic anhydride was heated to reflux under nitrogen. After ca. 5 min of reflux an intense dark red colour of the solution developed and remained unchanged for nearly one hour. Upon attempted isolation of this red product in the pure state, the selenide 71, its dimer 72 and some polymeric materials were obtained. If the reaction was run in the presence of 180 mg (1.04 mmol) of N-phenylmaleimide for 3 hours under reflux, the reaction mixture turned dark orange. After cooling, the solvent was evaporated in vacuo and to the resulting residue 1 ml of benzene was added to remove the unreacted N-phenylmaleimide. From the residue, 92 mg (24 %) of the NPM-adduct of 84 was obtained after recrystallization from benzene, m.p. 229-233°C. Lit.³³: m.p. 231-232°C, 57 %. NMR spectrum confirmed that the dienophile addition took place at the methyl-substituted thiophene ring. NMR (CDCl₃): δ (ppm) 7.58-7.15 (m, 5H, C₆H₅), 7.40 (s, 2H, selenophene), 3.30 (s, 2H, CH), 2.09 (s, 6H, CH₃). The singlet at δ 3.30 indicates an exo configuration of the adduct, since the deshielding effect of the sulfur bridge in the endo adduct would be more pronounced. Preparative TLC did not afford the endo adduct of 84.

Reductive debromination of the selenium dibromide 81. To 10 ml of 40 % sodium hydroxide solution cooled to 0°C, 377 mg (1.00 mmol) of the selenium dibromide 81 was added with stirring under nitrogen. The yellow dibromide decomposed within a few minutes forming white, milky emulsion. Upon addition of 4 ml of benzene to the emulsion, the selenolothiophene 84 was released into the organic phase, as followed by the appearance of a red-pink colour of the benzene layer. This process could be followed by NMR when a few drops of NaOD in D₂O were added to a solution of the dibromide in CDCl₃. After shaking of the NMR-tube for 20 seconds, the initially observed signals of the dibromide at 4.95 and 2.28 diminished, while four new singlets at δ (ppm) 10.04, 3.75, 2.65 and 2.20 appeared. We attribute these signals to the nonclassical selenolothiophene 84: 10.04 (s, 2H, H₄ and H₆), 2.65 (s, 6H, CH₃) and to the selenide 71: 3.75 (s, 4H, CH₂), 2.20 (s, 6H, CH₃). Integration over the methyl signals gave the ratio of 84:81:71 = 1:3:5. After one hour in the NMR-tube, the signal at 10.04 vanished and some new signals in the methylene region, probably originating from decomposition products, appeared.

4,6-Dimethyl-1H,3H-selenolo[3,4-c]thiophene (89). To a suspension of 13.2 g (0.0550 mol) of sodium sulfide nonahydrate in 350 ml of 95 % ethanol, 12.8 g (0.0500 mol) of solid 3,4-bis(chloromethyl)-2,5-dimethyl-selenophene (5) was added in small portions during 5 hours at room temperature. After stirring over-night, the precipitated solid was filtered off and washed with warm ethanol, the filtrate was concentrated to ca. 150 ml and poured into 0.5 l of water. The white suspension formed was extracted with chloroform, the combined chloroform extracts were washed with water, dried over magnesium sulfate and concentrated in vacuo to give 5.1 g (47 %) of a white, crystalline residue, m.p. 81-86°C.

Recrystallization from methanol gave 4.8 g (44 %) of the analytically pure sample of the title compound, m.p. 93-95°C. NMR (CDCl₃): δ (ppm) 3.66 (s, 4H, CH₂), 2.31 (s, 6H, CH₃), $^3J_{\text{Se-CH}_2} = 9.9$ Hz. In the mass spectrum, the peaks centred at m/e 218 (M⁺ and base peak), showed the same pattern as a spectrum simulated for one selenium and one sulfur atom. Anal. Calcd. for C₈H₁₀SSe: C 44.24; H 4.64; Se 36.35. Found: C 43.88; H 4.53; Se 35.49.

Extraction of the precipitated solid from above with boiling chloroform, evaporation and drying afforded 1.2 g (11 %) of the dimeric 1,3,7,9-tetramethyl-4H,6H,10H,12H-diselenolo[3,4-c:3',4'-h][1,6]dithiecin (90), m.p. 228-232°C, after recrystallization from pyridine/water (10:1). Owing to its low solubility in ordinary organic solvents, no NMR spectrum could be obtained. In the mass spectrum, the peaks centred at m/e 436 (M⁺) and at m/e 218 (base peak), showed the same pattern as a spectrum simulated for two sulfur and two selenium atoms and for one sulfur and one selenium atom, respectively.

4,6-Dicarbomethoxy-1H,3H-selenolo[3,4-c]thiophene (91). To a solution of 800 mg (3.33 mmol) of sodium sulfide nonahydrate in 200 ml of methanol, a solution of 1.30 g (3.00 mmol) of 3,4-bisbromomethyl-2,5-dicarbomethoxyselenophene (9) in 50 ml of tetrahydrofuran was added dropwise with stirring during 3 hours at room temperature. After stirring over-night, the reaction mixture was poured into 1.5 l of water and extracted several times with ether. The organic phase extracts were washed with water, dried over magnesium sulfate and concentrated. The half-crystalline residue obtained was recrystallized from methanol to give 678 mg (74 %) of the title compound, m.p. 183-185°C. NMR (CDCl₃):

δ (ppm) 4.09 (s, 4H, CH₂), 3.86 (s, 6H, CH₃). Anal. Calcd. for C₁₀H₁₀O₄SSe: C 39.35; H 3.30; Se 25.87. Found: C 38.48; H 3.29; Se 25.79.

No dimeric compound 92 was found. If the reaction was carried out in ethanol, a mixture of dimethyl and diethyl esters was formed. The transesterification was not complete even after 2 hours of reflux and the mixture of the two esters was not separated.

4,6-Dimethyl-1H,3H-selenolo[3,4-c]thiophene-2-oxide (93). A solution of 2.18 g (0.0100 mol) of the sulfide 89 in a mixture of 300 ml of methanol and 25 ml of water was cooled to 5°C and a 0.5 M solution of 2.35 g (0.0110 mol) of sodium metaperiodate in water was added dropwise with stirring. After stirring over-night, the precipitated sodium iodate was filtered off and the light-yellow filtrate was concentrated in vacuo to ca. 80 ml and left over-night in a refrigerator. The precipitated, light-yellow needles (340 mg) were filtered off and dried to give an analytically pure sample of the title sulfoxide, m.p. 132-133°C. Evaporation of the filtrate gave an additional 1.75 g (90 %) of the sulfoxide, m.p. 127-131°C. NMR (CDCl₃): δ (ppm) 4.04 (d, 2H, CH₂), 3.84 (d, 2H, CH₂), 2.41 (s, 6H, CH₃), $J_{\text{gem.}} = 15.0$ Hz. In the mass spectrum, the peaks centred at m/e 234 (M⁺) and at m/e 218 (M⁺-O, base peak), showed the same pattern as a spectrum simulated for one selenium and one sulfur atom. Anal. Calcd. for C₈H₁₀OSSe: C 41.20; H 4.32; Se 33.86. Found: C 40.87; H 4.26; Se 34.15.

4,6-Dicarbomethoxy-1H,3H-selenolo[3,4-c]thiophene-2-oxide (94). To a solution of 305 mg (1.00 mmol) of the sulfide 84 in a mixture of 30 ml of methanol and 4 ml of water cooled to 5°C, a 0.5 M solution of 235 mg (1.10 mmol) of sodium metaperiodate in water was added dropwise with stirring under nitrogen. After stirring over-night, the precipitated

sodium iodate was filtered off and the filtrate was concentrated in vacuo until a yellow suspension formed. After standing over-night, the precipitated sulfoxide was filtered off and dried, to give 212 mg (66 %) of the light-yellow crystals, m.p. 167-170°C (dec.).

NMR (CDCl₃): δ (ppm) 4.66 (d, 2H, CH₂), 4.47 (d, 2H, CH₂), 3.96 (s, 6h; CH₃), $J_{\text{gem.}}$ = 15.8 Hz. No satisfactory elemental analysis could be obtained.

Adduct of 4,6-dimethylselenolo[3,4-c]thiophene (95) with N-phenylmaleimide. A mixture of 350 mg (1.50 mmol) of the sulfoxide 93, 300 mg (1.73 mmol) of N-phenylmaleimide and 5 ml of freshly distilled, degassed acetic anhydride was heated to reflux under nitrogen during 4 hours. The colour changed to dark orange after the first hour of reflux. Upon cooling, 120 mg (47 %) of white needles, m.p. 287-289°C, after recrystallization from benzene/cyclohexane, precipitated. Mass spectrum confirmed the structure of the NPM-adduct showing major peaks at m/e 389 (M^+ , 6 %), 307 ($M^+ - H_2Se$, 100 %), 292 ($M^+ - H_2Se - CH_3$, 18 %), 216 ($M^+ - NPM$, 23 %). Unfortunately, no NMR spectrum could be recorded owing to the very low solubility of the adduct in ordinary organic solvents. NMR spectrum in warm DMSO-d₆ indicated the presence of only some decomposition products.

5,7-Dimethylselenolo[3,4-d][1,2]dithiane (100). To a solution of sodium disulfide, prepared from 6.7 g (0.028 mol) of sodium sulfide nonahydrate and 0.96 g (0.030 mol) of sulfur in 400 ml of 95 % ethanol, a solution of 6.4 g (0.025 mol) of 3,4-bis(chloromethyl)-2,5-dimethylselenophene (5) in 100 ml of tetrahydrofuran was added dropwise during two hours. After stirring over-night, the reaction mixture was poured into 1 l of water and the white suspension formed was extracted several times with chloroform. The combined chloroform extracts were washed with water, dried over magnesium sulfate and concentrated to give 5.6 g (90 %) of the

title compound, m.p. 224-228°C. An analytically pure sample was obtained by recrystallization from toluene, m.p. 230-230.5°C. Owing to the low solubility of the compound in ordinary organic solvents, no NMR spectrum could be recorded. In the mass spectrum, the peaks centred at m/e 250 (M^+), showed the same pattern as a spectrum simulated for one selenium and two sulfur atoms. Anal. Calcd. for $C_8H_{10}S_2Se$: C 38.55; H 4.04; Se 31.68. Found: C 39.39; H 4.14; Se 30.62.

92 % of the dithiane could be recovered after 2 hours of reflux with methanolic sodium methoxide solution.

5,7-Dicarbomethoxyselenolo[3,4-d][1,2]dithiane (101). To a solution of sodium disulfide, prepared from 1.3 g (5.5 mmol) of sodium sulfide nonahydrate and 0.18 g (5.6 mmol) of sulfur in 160 ml of 95 % ethanol, a solution of 2.17 g (5.01 mmol) of 3,4-bisbromomethyl-2,5-dicarbomethoxy-selenophene (9) in 80 ml of tetrahydrofuran was added dropwise with stirring during 2 hours. After stirring over-night the reaction mixture was poured into 1 l of water and the white suspension formed was extracted with chloroform. The chloroform extracts were washed with water, dried over magnesium sulfate and concentrated to give 1.2 g (71 %) of the title compound, m.p. 163-165°C after recrystallization from ethanol. In the mass spectrum, the peaks centred at m/e 338 (M^+), showed the same pattern as a spectrum simulated for two sulfur and one selenium atom.

NMR ($CDCl_3$): δ (ppm) 4.41 (s, 4H, CH_2), 3.86 (s, 6H, CO_2CH_3).

Anal. Calcd. for $C_{10}H_{10}O_4S_2Se$: C 35.61; H 2.99; Se 23.41. Found: C 35.67; H 3.08; Se 23.26.

Although reflux of the dithiane with methanolic sodium methoxide solution brought about the decomposition of the compound, no formation of the selenolothiophene 96 could be observed. Neither could any adducts

be trapped if the reaction was carried out in the presence of N-phenylmaleimide or dimethyl acetylene dicarboxylate. Anal. Calcd. for $C_{10}H_{10}N_2Se$: C 50.64; H 4.25; Se 33.29. Found: C 50.58; H 4.37; Se 33.26.

3,4-Biscyanomethyl-2,5-dimethylselenophene (103). To a solution of 4.0 g (0.081 mol) of sodium cyanide in 75 ml of dimethyl sulfoxide, 10.3 g (0.0402 mol) of solid 3,4-bischloromethyl-2,5-dimethylselenophene (5) was added in small portions with stirring and external cooling. During the reaction, the temperature was held under $35^{\circ}C$. After complete addition, the reaction mixture was stirred for 20 min and poured into ice-water. The precipitated light-brown crystals were filtered off and recrystallized from ligroin, to give 8.6 g (90 %) of the title compound, as colourless large prisms, m.p. $125-127^{\circ}C$. NMR ($CDCl_3$): δ (ppm) 3.57 (s, 4H, CH_2), 2.46 (s, 6H, CH_3), $^3J_{-77Se-CH_2} = 10.6$ Hz.

3,4-Dicarbethoxymethyl-2,5-dimethylthiophene (104). A mixture of 1.90 g (10.0 mmol) of 3,4-biscyanomethyl-2,5-dimethylthiophene (102),³⁷ 1.0 g (22 mmol) of ethanol, 4.2 g (22 mmol) of p-toluenesulfonic acid monohydrate and 30 ml of mesitylene was heated to reflux during 3 hours, cooled and poured into 50 ml of water. The phases were separated, the water phase was extracted with benzene, the combined organic phases were washed with sodium bicarbonate solution and water, dried over magnesium sulfate and concentrated. The light-brown oil obtained was fractionated at 1.0 mm Hg and a broad fraction, $150-158^{\circ}C$, was collected. Recrystallization from petroleum ether (b.p. $40-60^{\circ}C$) gave 2.5 g (88 %) of colourless needles, m.p. $31-33^{\circ}C$. Lit.³⁷: b.p. $137-140^{\circ}C/1$ mm Hg; 45 %.

3,4-Dicarbethoxymethyl-2,5-dimethylselenophene (105). A mixture of 2.37 g (10.0 mmol) of 3,4-biscyanomethyl-2,5-dimethylselenophene (103),

1.0 g (22 mmol) of ethanol, 4.2 g (22 mmol) of p-toluenesulfonic acid monohydrate and 25 ml of mesitylene was heated to reflux during 2.5 hours, cooled and poured into 50 ml of water. The phases were separated, the water phase was extracted once with benzene, the combined organic phases were washed with sodium bicarbonate solution and water, dried over magnesium sulfate and concentrated. The light-brown, oily residue obtained solidified on standing in a refrigerator. Recrystallization from petroleum ether (b.p. 40-60°C) afforded 2.8 g (85 %) of the title compound, m.p. 49-50°C, as colourless needles. NMR (CDCl₃): δ (ppm) 4.10 (q, 6H, CH₃), 3.49 (s, 4H, CH₂), 2.41 (s, 6H, CH₃), 1.23 (t, 6H, CH₃), $J_{\text{CH}_2-\text{CH}_3} = 7.0$ Hz. Anal. Calcd. for C₁₄H₂₀O₄Se: C 50.76; H 6.08; Se 23.83. Found: C 50.82; H 5.99; Se 24.01.

2,5-Bisbromomethyl-3,4-dicarbethoxythiophene (106). To a solution of 1.42 g (5.00 mmol) of the thiophene 104 in 30 ml of dry carbon tetrachloride, 1.85 g (10.4 mmol) of dry N-bromosuccinimide and ca. 50 mg of azobisisobutyronitrile were added all at once and the reaction mixture was refluxed for one hour. The succinimide formed was removed by hot filtration, the filtrate was concentrated in vacuo and the half-crystalline residue obtained was recrystallized from ligroin to give 1.5 g (68 %) of light-yellow crystals, m.p. 48-51°C. NMR (CDCl₃): δ (ppm) 4.66 (s, 4H, CH₂Br), 4.08 (t, 4H, CH₂), 3.63 (s, 4H, CH₂), 1.22 (t, 6H, CH₃), $J_{\text{CH}_2-\text{CH}_3} = 7.0$ Hz. Anal. Calcd. for C₁₄H₁₈Br₂O₄S: C 38.03; H 4.10; S 7.25. Found: C 37.65; H 4.01; S 8.08.

3,4-Dibromo-2,5-diphenylselenophene. To a suspension of 2.83 g (10.0 mmol) of 2,5-diphenylselenophene⁹ in 200 ml of acetic acid cooled to 15°C, a solution of 3.6 g (22.5 mmol) of bromine in 50 ml of acetic acid was added dropwise with stirring. After 3 hours of stirring at room

temperature, during which time most of the solid dissolved, the reaction mixture was poured into 1 l of cold water, the light-yellow precipitate was filtered off and recrystallized from ethanol to give 4.2 g (95 %) of the title compound, m.p. 104-106°C. NMR (CDCl₃): δ (ppm) 7.66-7.32 (m. C₆H₅). Anal. Calcd. for C₁₆H₁₀Br₂Se: C 43.57; H 2.29; Se 17.90. Found: C 43.70; H 2.29; Se 17.99.

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REFERENCES

- ¹S. Gronowitz and A. Konar, J. Chem. Soc. Chem. Commun. 163 (1977).
- ²M.P. Cava and M.V. Lakshmikantham, Acc. Chem. Res. 8, 139 (1975).
- ³K.T. Potts, "Special Topics in Heterocyclic Chemistry"; Eds.
A. Weissberger and E.C. Taylor; Chapter 6, Wiley, New York 1977.
- ⁴C.A. Ramsden, Tetrahedron 33, 3203 (1977)
- ⁵B.E. Maryanoff, J. Stackhouse, G.H. Senkler, Jr. and K. Mislow,
J. Am. Chem. Soc. 97, 2718 (1975).
- ⁶J. Stackhouse, G.H. Senkler, Jr., B.E. Maryanoff and K. Mislow,
J. Am. Chem. Soc. 96, 7835 (1974).
- ⁷C.J. Horner, L.E. Saris, M.V. Lakshmikantham and M.P. Cava,
Tetrahedron Lett. 2581 (1976).
- ⁸L.E. Saris and M.P. Cava, J. Am. Chem. Soc. 98, 867 (1976).
- ⁹S. Gronowitz and A. Konar, Chemica Scripta 12, 11 (1977).
- ¹⁰D.J. Zwanenburg and H. Wynberg, Rec. trav. chim. Pays-Bas 88, 321 (1969).
- ¹¹D.L. Klayman and T.S. Griffin, J. Am. Chem. Soc. 95, 197 (1973).
- ¹²H.J. Backer and W. Stevens, Rec. trav. chim. Pays-Bas 59, 423 (1940)
- ¹³M. Cinquini, S. Colonna and R. Giovini, Chem. and Ind. 1737 (1969).
- ¹⁴P. Heimbach and R. Schimpf, Angew. Chem. 81, 186 (1969).
- ¹⁵S. Tamagaki, R. Akatsuka and S. Kozuka, Bull. Soc. Chem. Japan 50,
1641 (1977).
- ¹⁶J. Sauer, Angew. Chem. 79, 76 (1967).

- ¹⁷A.G. Williams and G.B. Butler, J. Org. Chem. 45, 1232 (1980).
- ¹⁸H. Wamhoff and K. Wald, Org. Preparations and Procedures Int. 7, 251 (1975).
- ¹⁹C. Müller, A. Schweig, M.P. Cava and M.V. Lakshmikantham, J. Am. Chem. Soc. 98, 7187 (1976).
- ²⁰R. Gleiter, R. Bartetzko, G. Brähler and H. Bock, J. Org. Chem. 43, 3893 (1978).
- ²¹Y. Wakatsuki, T. Kuramitsy and H. Yamazaki, Tetrahedron Lett. 4549 (1974).
- ²²H.D. Hartough, "Thiophene and Its Derivatives"; Ed. A. Weissberger; Interscience Publishers Inc., New York 1952, p. 48 and following pages.
- ²³M. Peyrot, D. Villesot and Y. Lepage, C. R. Acad. Sci., Ser. C 282, 607 (1976).
- ²⁴N.N. Magdesieva and N.S. Zefirov in "Organic Selenium Compounds: Their Chemistry and Biology"; Eds. D.L. Klayman and W.H.H. Günther; Chapter XI B, p. 433, Wiley-Interscience, New York, 1973.
- ²⁵L. Lepage and Y. Lepage, J. Heterocyclic Chem. 15, 1185 (1978).
- ²⁶Ya.L. Goldfarb and M.S. Kondakova, Izv. Akad. Nauk SSSR 495 (1956).
- ²⁷M.P. Cava, M.A. Sprecker and W.R. Hall, J. Am. Chem. Soc. 96, 1817 (1974).
- ²⁸A. Schönberg and R.C. Azzam, J. Chem. Soc. 1428 (1939).
- ²⁹W. Ried and R. Conte, Chem. Ber. 104, 1573 (1971).
- ³⁰E.C. Taylor, G.H. Hawks, III and A. McKillop, J. Am. Chem. Soc. 90, 2421 (1968).
- ³¹K. Dimroth, G. Pohl and H. Follmann, Chem. Ber. 99, 634 (1966).
- ³²H. Wynberg and D.J. Zwanenburg, J. Org. Chem. 29, 1919 (1964).

- ³³L.E. Saris and M.P. Cava, Heterocycles 6, 1349 (1977).
- ³⁴G. Cignarella and G. Cordella, Tetrahedron Lett. 1871 (1973).
- ³⁵G. Cignarella and G. Cordella, Gazz. Chim. Ital. 104, 455 (1974).
- ³⁶L. Friedman and H. Schechter, J. Org. Chem. 25, 877 (1960).
- ³⁷R. Helmers, J. prakt. Chem. 313, 31 (1971).
- ³⁸see H. Henecka in "Methoden der organischen Chemie" (Houben-Weyl), 4th edition, Vol. 8, p. 536, Georg Thieme Verlag, Stuttgart 1952.
- ³⁹F.L. James and W.H. Bryan, J. Org. Chem. 23, 1225 (1958).
- ⁴⁰L.C. King and G.K. Ostrum, J. Org. Chem. 29, 3459 (1964).
- ⁴¹F. Langer and F. Wessely, Monatsh. Chem. 86, 887 (1955).

Paper K

On the Reaction of 1,4-Diketones with Phosphorus Pentaselenide.

On the Reaction of 1,4-Diketones with Phosphorus Pentaselenide

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Abstract

On the reaction of 1,4-diketones with phosphorus pentaselenide. Gronowitz, S.; Konar, A. (Division of Organic Chemistry 1, Chemical Center, University of Lund, P.O. Box 740, S-220 07 Lund, Sweden). *Chemica Scripta* (Sweden) 1977, 12 (1), 11–14.

Phosphorus pentaselenide prepared from red, amorphous selenium was shown to be sufficiently reactive towards 1,4-diketones to effect their cyclization to 2,5-disubstituted selenophenes in moderate yields. Thus, 2,5-hexanedione was cyclized in 38 % yield to give 2,5-dimethylselenophene, the two butanediones V were cyclized in ca. 50 % yield to give the two corresponding 2,5-diphenyl-substituted selenophenes, and even cyclization of tetrabenzoylthane I could be accomplished in 40 % yield to give the mixture of the selenides IV together with some other products. This reaction can therefore be considered as a more general way to 2,5-disubstituted selenophenes than previously realized.

Introduction

The possible existence of phosphorus pentaselenide was suggested by Berzelius [1] as early as 1834, and claims to its preparation [2] date back to 1862. It appears much less reactive towards organic species than the analogous phosphorus pentasulfide, which is widely used for the preparation of organosulfur compounds and sulfur-containing organophosphorus materials, in such reactions as *e.g.* conversion of oxo to thio heterocyclic compounds or conversion of amides to thioamides. However, even in synthesizing these compounds by the use of phosphorus pentasulfide, considerable difficulty may be encountered on many occasions. These problems are greatly augmented in working with phosphorus pentaselenide, possibly because this poorly characterized reagent is often useless unless freshly prepared. Since there are no specific ways of characterizing P_2Se_5 , variations in reagent quality may have contributed much to the confusion that exists in regard to its use.

The first thorough review of the preparation and physical properties of phosphorus pentaselenide appeared in 1968 [3]. However, a systematic study of reaction conditions, solvents, temperatures, and potential catalysts was lacking until 1976, when Zingaro *et al.* [4] employed phosphorus pentaselenide for the direct selenation of pyrimidines. The reaction parameters which were varied for the purpose of maximizing the yield of selenated pyrimidine included reaction time, reaction temperature, nature of the functional group in the organic substrate, the solvent system, the extent of the subdivision of the phosphorus pentaselenide used, and the position to be substituted on the pyrimidine ring.

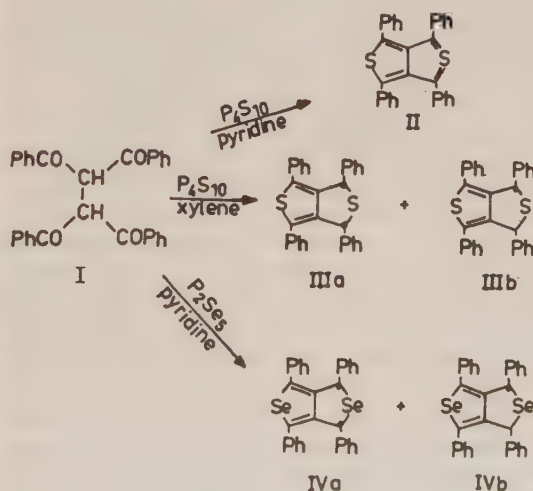
The preparation of phosphorus pentaselenide, as described in 1968 by Zingaro *et al.* [3], consists of heating stoichiometric amounts of dry red phosphorus and grey selenium powder to 450 °C for 12 hours in an atmosphere of nitrogen in a sealed, heavy-walled ampoule. The resulting insoluble, black-purple solid was then powdered in a ball-mill under an inert atmosphere and stored over P_2O_5 . Older procedures [2,5,6] were reported to give a much less active product [3].

There are few reports in the literature concerning the reactions of phosphorus pentaselenide with organic compounds. The most extensively studied one appears to be the reaction of P_2Se_5 with alcohols [2,3,7–11], but reactions between P_2Se_5 and amines [12, 13], amides [14, 15], ureas [16], phenyl isocyanate [17], carbon tetrachloride [5, 18] and carbonyl compounds [19–21] have also been reported.

The reaction of phosphorus pentasulfide with 1,4-dicarbonyl compounds is a well-established synthetic route to 2,5-disubstituted thiophenes, known as the Paal-Knorr synthesis [22]. The only example of using phosphorus pentaselenide for a similar preparation of a 2,5-disubstituted selenophene is, to the best of our knowledge, its reaction with 2,5-hexanedione described by Paal nearly 100 years ago [19]. 2,5-Dimethylselenophene obtained in this way was also the first compound in the selenophene series, as unsubstituted selenophene was obtained much later. In the recent review of the chemistry and biology of organic selenium compounds [23], the reaction of P_2Se_5 with 1,4-dicarbonyl compounds is not even mentioned as a possible way of synthesizing simple selenophenes. Another example of employing P_2Se_5 for a ring-closure reaction to give a selenium-containing five-membered heterocycle is the first preparation of 2,5-dimethyl- and 2,5-diphenyl-1,3,4-selenodiazoles from the corresponding hydrazines [20].

Results and discussion

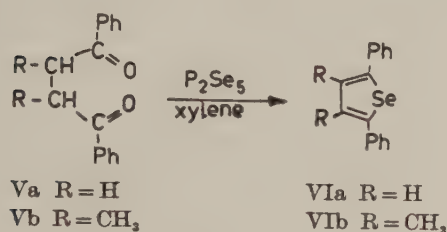
In our studies of the non-classical selenophenes [24], we were interested in a preparation of a stable derivative of the selenolo-[3,4-c]selenophene system. Since the only stable derivative of an analogous sulfur compound turned out to be its tetraphenyl derivative II, prepared in *one* step in the reaction of phosphorus pentasulfide in pyridine with tetrabenzoylthane (I) [25], we quite naturally chose a similar route to tetraphenylselenolo-[3,4-c]selenophene.



Our early trials to react tetrabenzoylthane (I) with phosphorus pentaselenide prepared according to Zingaro *et al.* [3] were unsuccessful and resulted in a partial recovery of the starting tetraketone along with some unidentified, non-selenium-containing polymeric materials. Numerous experiments to optimize reaction conditions were carried out, but no organic, selenium containing products could be isolated.¹

We attributed this failure to some extent to the insolubility of phosphorus pentaselenide, but mainly to its unsatisfactory quality and insufficient reactivity in this reaction. This was supported by the fact that the phosphorus pentaselenide used here could be employed in the reaction with 2,5-hexanedione, where 2,5-dimethylselenophene was obtained in 19 % yield [26].

Reactions with two other 1,4-dicarbonyl compounds, 1,4-diphenyl-1,4-butanedione (Va) and 2,3-dimethyl-1,4-diphenyl-1,4-butanedione (Vb) led again to the recovery of starting materials along with some unidentified polymers.



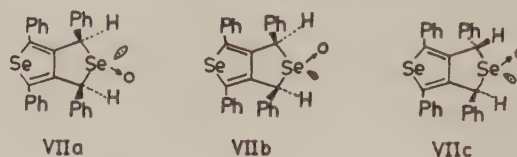
These facts confirmed our belief that the reactivity of the phosphorus pentaselenide must be improved in order to effect its reaction with 1,4-dicarbonyl compounds. A slight modification of the procedure of Zingaro *et al.* [3], in which red selenium prepared according to Campbell *et al.* [27] was used instead of the grey form, yielded phosphorus pentaselenide of such quality, that the ring-closure of both butanediones V, as well as the ring-closure of tetrabenzoylthane (I), could be accomplished. Even the yield of 2,5-dimethylselenophene could be raised from 19 to 38 %. The yields of 2,5-diphenylsubstituted selenophenes VIa and VIb were quite satisfactory, 58 % and 48 %, respectively.

2,5-Diphenylselenophene (VIa) was previously prepared in 65 % yield in the reaction of 1,4-diphenyl-1,3-butadiene with gaseous hydrogen selenide in the presence of catalytic amounts of silver acetate [28]. We found that the use of ethanolic sodium hydrogen selenide [29] was an excellent means to circumvent the considerable difficulties in handling gaseous H_2Se , and in addition gave an even better yield of VIa (cf. Experimental part).

3,4-Dimethyl-2,5-diphenylselenophene (VIb) was first prepared by Wakatsuki *et al.* [30] in the reaction of a cobalto-cyclopentadiene complex with selenium in 65 % yield. We have later prepared VIb by reacting red elemental selenium with 2,3-dimethyl-1,4-diphenyl-1,3-butadiene in 52 % yield. VIb prepared now by the ring-closure of the diketone Vb with P_2Se_5 , showed the same melting point and spectroscopic data as the selenophene from the reaction mentioned above.

The reaction of tetrabenzoylthane (I) with phosphorus pentasulfide takes different courses depending on the solvent used. The mixture of *cis*- and *trans*-sulfides III was obtained when xylene was employed as a solvent [31], while the reaction in pyridine led directly to the non-classical tetraphenylthieno-[3,4-*c*]thiophene (II) in high yield [25]. We have, analogously, carried out the reaction between I and P_2Se_5 in both xylene and pyridine, but no formation of the non-classical tetraphenylselenolo[3,4-*c*]selenophene could be observed. In both cases we could isolate the mixture of *cis*- and *trans*-selenides IV, which were formed in a slightly higher yield in pyridine than in xylene. Column chromatography of the crude reaction product on silica gel also afforded minor amounts of 3-benzyl-2,5-diphenyl-

selenophene and 3,4-dibenzyl-2,5-diphenylselenophene. Only the former compound was obtained in amounts that allowed its purification and full spectral identification. We also obtained an almost identical product distribution in the reaction of phosphorus pentaselenide with 3,4-dibenzoyl-2,5-diphenylfuran. The isomeric mixture of the two selenides IV was separated by ptlc on silica gel, but even short column chromatography according to Hunt and Rigby [32] could be successfully employed, as well as fractional crystallization from ethanol/cyclohexane. The readily isolable major isomer (m.p. 186–187 °C) and the difficultly isolable minor isomer (m.p. 159–161 °C) were formed in a ratio of 9:1. An attempt to assign *cis*- or *trans*-configurations to the isomeric selenides IV was made on the basis of the NMR spectra of their selenoxides, in analogy to the assignments made by Cava *et al.* [31] for the sulfides III. Thus, hydrogen peroxide oxidation of the major, high-melting isomer, gave a single selenoxide (m.p. 200–202 °C, decomp.) in 85 % yield. The same product was also obtained in 80 % yield, when the mixture of the two selenides IV was oxidized, which could indicate that only the less hindered *cis*-selenide had reacted. The NMR spectrum of the *cis*-selenoxide was expected to show only one signal for the two equivalent benzylic hydrogens assuming that only one, less hindered *cis*-selenoxide VIIa, was formed.



The recorded NMR spectrum in warm DMSO showed, however, two singlets at δ 6.34 and 5.55. Due to the very low solubility of the selenoxide in all commercially available deuteriated solvents, the area measurements of the benzylic hydrogens signals could not be made with the usual accuracy, but nevertheless a significant area difference could be observed. The non-equivalent benzylic hydrogens of the *trans*-selenoxide VIIc are expected to show different shifts, but exactly the same areas. These facts, together with a comparison with the properties of the *cis*-sulfoxide IIIa [31], which in the same way as the above selenoxide was the major, high-melting, less soluble isomer, make more likely the suggestion that the two observed signals represent the two forms VIIa and VIIb of the *cis*-selenoxide, rather than the single *trans*-form VIIc.

An attempt to confirm this suggestion by warming the selenoxide solution to overcome the inversion barrier on the selenium atom led to the decomposition of the selenoxide with development of a deep blue-green colour and considerable broadening of the two singlets. This behaviour perhaps indicates the formation of the non-classical selenolo[3,4-*c*]selenophene system, which will be the subject of a subsequent report.

Unfortunately, oxidation of the minor, low-melting isomer of the selenide pair IV could not be achieved by hydrogen peroxide in refluxing THF, and the use of more powerful oxidizing agents led to the decomposition of the starting material. Therefore, we were not able to record the NMR spectrum of any other selenoxide, which made a structural assignment uncertain.

Experimental

Diphosphorus pentaselenide was prepared by a slight modification of the method of Zingaro *et al.* [3, 4]. The red, amorphous selenium used was prepared according to Campbell *et al.* [27] by the acid hydrolysis of an aqueous solution of potassium selenocyanate. Both selenium and red phosphorus were washed with methanol and anhydrous ether and then dried for a week in vacuo over phosphorus pentoxide. Stoichiometric amounts

of dry phosphorus and selenium were placed in an electric mill and mixed intimately during 0.5 h, with water cooling of the mill. The mixture was transferred to a heavy-walled glass ampoule, which was evacuated and then filled with nitrogen and sealed. The sealed ampoule was placed in a screw-cap iron cylinder which was heated to 450 °C for 16 h with rocking.

As rapid cooling of the reaction mixture probably renders a more reactive product, the ampoule was removed from the metal cylinder while the phosphorus selenide formed was still liquid, and allowed to cool to room temperature before it was broken. The black-purple, glassy solid obtained was stored in a desiccator over P_2O_5 , and ground into a very fine powder just prior to use. In most cases, the entire amount of P_2Se_5 was used within a few days after preparation, as reagent older than 2 weeks becomes almost totally inactive.

2,5-Dimethylselenophene. A mixture of 22.8 g (0.2 mol) of 2,5-hexanedione, 36.5 g (0.08 mol) of finely powdered phosphorus pentaselenide and 25 ml of xylene was placed in a heavy-walled glass ampoule, which was sealed and heated in a closed stainless steel cylinder at 190 °C overnight. After cooling, the ampoule was broken and the contents poured into 300 ml of 5 N NaOH and steam-distilled. The organic layer was separated and the water phase was extracted with chloroform. The combined organic phases were dried over magnesium sulfate, concentrated and distilled to give 12.1 g (38 %) of 2,5-dimethylselenophene, b.p. 155–157 °C (lit. [19] b.p. 153–155 °C).

The same reaction with phosphorus pentaselenide prepared according to ref. 2 gave only 19 % yield [26].

2,5-Diphenylselenophene (VIa). A mixture of 11.9 g (0.05 mol) of dibenzoylthane, 9.1 g (0.02 mol) of phosphorus pentaselenide and 160 ml of mesitylene was refluxed for 4 h, cooled and poured into 250 ml of 5 N NaOH. The organic layer was separated, the dark residue was extracted several times with chloroform, the combined organic phases were dried over magnesium sulfate and concentrated, giving a half-crystalline residue. Recrystallization from ethanol gave 7.5 g (53 %) of the title compound, m.p. 174–177 °C (lit. [28] m.p. 171 °C).

2,5-Diphenylselenophene from 1,4-diphenyl-1,3-butadiyne. To a colourless solution of 15 mmol of sodium hydrogen selenide in 50 ml of abs. ethanol prepared according to ref. 29, 1.41 g (7 mmol) of 1,4-diphenyl-1,3-butadiyne [33] and 5 mg of silver acetate were added, whereupon the reaction mixture was refluxed in a nitrogen atmosphere until the diyne absorption in the IR spectrum had disappeared (5 h). The reaction mixture was then poured into 250 ml of ice-cold 2 N hydrochloric acid and the precipitate formed was filtered, dissolved in chloroform, and decolourized with active carbon. The chloroform solution was dried over magnesium sulfate and concentrated to give 1.5 g (76 %) of yellow crystals with m.p. 171–174 °C. M.p. 175–177 °C after recrystallization from ethanol (lit. [28] 171 °C).

3,4-Dimethyl-2,5-diphenylselenophene (VIb). A mixture of 2.64 g (0.01 mol) of 2,3-dimethyl-1,4-diphenyl-1,4-butanedione [34], 1.83 g (0.004 mol) of phosphorus pentaselenide and 80 ml of mesitylene was refluxed for 4 h, cooled and poured into 150 ml of 5 N NaOH. The organic layer was separated, the dark residue was extracted several times with chloroform, the combined organic phases were dried over magnesium sulfate and concentrated to give a half-crystalline residue. Recrystallization from ligroin gave 1.5 g (48 %) of the title compound, m.p. 157.5–158 °C. NMR spectrum ($CDCl_3$): δ = 7.30–7.50 (m, $2 \times Ph$, 10H); δ = 2.16 (s, $2 \times CH_3$, 6H). In the mass spectrum the peaks centred at m/e 312 (M^+ and base peak) showed the same pattern as a spectrum simulated for one selenium atom. [Found: C 70.09; H 5.24; Se 24.66; M.wt. 312. Calc. for $C_{16}H_{18}Se$: C 69.45; H 5.18; Se 25.36; M.wt. 311.29.]

1,3,4,6-Tetraphenyl-1H,3H-selenolo[3,4-c]selenophene (IV). A suspension of 2.2 g (5 mmol) of tetrabenzoylthane [31] and 1.83 g (4 mmol) of phosphorus pentaselenide in 30 ml of dry

pyridine was heated at 220 °C in a sealed, heavy-walled glass ampoule placed in a closed metal cylinder for 17 hours. The ampoule was then broken, the excess of phosphorus pentaselenide was filtered and the light-brown filtrate was poured into 50 ml of 5 N sodium hydroxide, whereupon the upper pyridine phase became very dark, but no precipitate could be observed. Acidification with 250 ml of ice-cold 2 N hydrochloric acid gave 1.3 g (48 %) of a red-brown amorphous precipitate, which was dissolved in a small amount of warm benzene and chromatographed on silica gel with cyclohexane/toluene as eluent. The mass spectrographic analysis of the first fractions indicated a mixture of 3-benzyl-2,5-diphenylselenophene (VIII) and 3,4-dibenzyl-2,5-diphenylselenophene (IX). Recrystallization from ethanol gave 100 mg (5 %) of yellow crystals of VIII, m.p. 125–126 °C. NMR spectrum ($CDCl_3$): δ = 7.17–7.50 (m, $3 \times Ph$, H_4 , 16H); δ = 3.98 (s, CH_2 , 2H). [Found: C 74.05; H 4.96; Se 21.05; M.wt. 374. Calc. for $C_{23}H_{18}Se$: C 73.99; H 4.86; Se 21.15; M.wt. 373.36.]

IX was formed in amounts not allowing its full spectral identification.

The later fractions eluted with an increasing toluene ratio in the eluent, afforded a mixture of the two selenides IV, which was subjected to ptlc on silica gel with cyclohexane:toluene 9:1 as eluent. Mass spectrographic analysis of the resulting three bands indicated (in the order of solubility): 3-benzyl-2,5-diphenylselenophene (VIII), m/e 374, a major isomer IV, m/e 542, and the minor isomer IV, m/e 542. Recrystallization from ethanol/cyclohexane afforded 950 mg (35 %) of the major selenide isomer, m.p. 186–187 °C, NMR spectrum ($CDCl_3$): δ = 7.04–7.16 (m, $4 \times Ph$, 20H), δ = 5.90 (s, $2 \times CH$, 2H). [Found: C 66.67; H 4.10; Se 29.22; M.wt. 542. Calc. for $C_{30}H_{22}Se_2$: C 67.21; H 4.10; Se 29.40; M.wt. 540.43] and 106 mg (4 %) of the minor selenide isomer, m.p. 159–161 °C, NMR spectrum ($CDCl_3$): δ = 7.01–7.22 (m, $4 \times Ph$, 20H); δ = 5.95 (s, $2 \times CH$, 2H).

1,3,4,6-Tetraphenyl-1H,3H-selenolo[3,4-c]selenophene 2-oxide (VII). 115 mg (1 mmol) of 30 % hydrogen peroxide was added to a solution of 541 mg (1 mmol) of the major selenide isomer IV in 5 ml of dry THF and the reaction mixture was stirred for 2 h at room temperature. The white precipitate formed was filtered and dried, giving 472 mg (85 %) of the selenoxide which melted at 200–202 °C, developing a deep, blue-green colour. NMR spectrum (warm $DMSO-d_6$): δ = 7.23–7.70 (m); δ = 6.34 (s); δ = 5.55 (s). Due to the very low solubility of the selenoxide, the area measurements were uncertain.

We attempted to oxidize the minor selenide isomer IV under the same conditions and in refluxing THF, but only unchanged starting material was recovered.

The 1H NMR spectra were obtained with a Varian A-60 and on a Jeol MH-100 high resolution spectrometer. The IR spectra were recorded on a Perkin-Elmer model 257 instrument. The gas chromatograph used was a Perkin-Elmer 900 instrument with flame ionization detector, connected to a Varian model 480 integrator. Mass spectra were obtained with an LKB 9000 mass spectrometer. Elementary analyses were carried out by Ilse Beetz, Mikroanalytisches Laboratorium, Kronach, Germany.

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References

1. See Gmelin's "Handbuch der Anorganischen Chemie", Sys. Nr. 9–12, Verlag Chemie, Weinheim/Bergstr. 1942, p. 244.
2. Carius, L. and Bogen, W., Ann. 1862, 124, 57.

3. Kudchadker, M. V., Zingaro, R. A. and Irgolic, K. J., *Can. J. Chem.* 1968, 46, 1415.
4. Mickey, C. D. and Zingaro, R. A., *Int. J. Sulfur Chem.* 1976, 8, 557.
5. Rathke, B., *Ann.* 1869, 152, 200.
6. Muthmann, W. and Clever, A., *Z. Anorg. Chem.* 1897, 13, 191.
7. Zemlyanskii, N. I. and Gorak, R. D., *Zh. Obshch. Khim.* 1971, 41, 1691.
8. Zemlyanskii, N. I. and Gorak, R. D., *Zh. Obshch. Khim.* 1971, 41, 2446.
9. Gorak, R. D., Zemlyanskii, N. I. and Muravev, I. V., *Zh. Obshch. Khim.* 1972, 42, 56.
10. Zemlyanskii, N. I., Gorak, R. D. and Kolodii, Ja. I., *Ukr. Khim. Zh.* 1973, 39, 68.
11. Ivanyutin, M. I., *Org. Reagenty Anal. Khim.* 1973, 44.
12. Melton, R. G. and Zingaro, R. A., *Can. J. Chem.* 1968, 46, 1425.
13. Mickey, C. D. and Zingaro, R. A., *Inorg. Chem.* 1973, 12, 2115.
14. Collard-Charon, C. and Renson, M., *Bull. Soc. Chim. Belges* 1963, 72, 304.
15. Jensen, K. A. and Nielsen, P. H., *Acta Chem. Scand.* 1966, 20, 597.
16. Jensen, K. A., Felbert, G. and Kägi, B., *Acta Chem. Scand.* 1966, 20, 281.
17. Collard-Charon, C. and Renson, M., *Bull. Soc. Chim. Belges* 1962, 71, 531.
18. Yarovenko, N. N., Gaziyeva, G. B., Shemanina, V. N. and Fedorova, N. A., *Zh. Obshch. Khim.* 1959, 29, 940.
19. Paal, C., *Chem. Ber.* 1885, 18, 2255.
20. Stolle, R. and Gutmann, L., *J. Prakt. Chem.* 1934, 69, 509.
21. van den Hende, J. H. and Klingsberg, E., *J. Am. Chem. Soc.* 1966, 88, 5045.
22. Hartough, H. D., "The Chemistry of Heterocyclic Compounds", Interscience Publishers, Inc. N.Y., 1952, p. 63.
23. "Organic Selenium Compounds: Their Chemistry and Biology", Edited by D. L. Klayman and W. H. H. Günther, John Wiley & Sons, Inc., 1973, Chapter XIB.
24. Gronowitz, S. and Konar, A., *J. Chem. Soc., Chem. Commun.* 1977, 163.
25. Cava, M. P., Sprecker, M. A. and Hall, W. R., *J. Am. Chem. Soc.* 1974, 96, 1817.
26. Frejd, T., Thesis, Lund 1975.
27. Campbell, T. W. and McCullough, J. D., *J. Am. Chem. Soc.* 1945, 67, 1965.
28. Curtis, R. F., Hasnain, S. N. and Taylor, J. A., *J. Chem. Soc., Chem. Commun.* 1968, 365.
29. Klayman, D. L. and Griffin, T. S., *J. Am. Chem. Soc.* 1973, 95, 197.
30. Wakatsuki, Y., Kuramitsy, T. and Yamazaki, H., *Tetr. Lett.* 1974, 4549.
31. Cava, M. P., Behforouz, M., Husbands, G. E. M. and Srinivasan, M., *J. Am. Chem. Soc.* 1973, 95, 2561.
32. Hunt, B. J. and Rigby, W., *Chem. Ind.* 1967, 1868.
33. Campbell, I. D. and Eglinton, G., *Org. Synth., Coll. Vol. V*, 517.
34. Perry, C. W., Kalnins, M. V. and Deitscher, K. H., *J. Org. Chem.* 1972, 37, 4371.

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